

Replication of Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes (LEADER trial)

NCT03936049

December 27, 2019

1. RCT Details

This section provides a high-level overview of the RCT that the described real-world evidence study is trying to replicate as closely as possible given the remaining limitations inherent in the healthcare databases.

1.1 Title

Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes ([LEADER](#) trial)

1.2 Intended aim(s)

The primary hypothesis was that liraglutide would be noninferior to placebo (plus standard of care) with regard to the primary outcome, with a margin of 1.30 for the upper boundary of the 95% confidence interval of the hazard ratio.

1.3 Primary endpoint for replication and RCT finding

Composite of Cardiovascular Death, Non-fatal Myocardial Infarction, or Non-fatal Stroke

1.4 Required power for primary endpoint and noninferiority margin (if applicable)

90% power and noninferiority margin of hazard ratio of 1.30

1.5 Primary trial estimate targeted for replication

HR = 0.87 (95% CI 0.78-0.97) comparing liraglutide to placebo (Marso et al.)

2. Person responsible for implementation of replication in Aetion

Ajinkya Pawar, Ph.D. implemented the study design in the Aetion Evidence Platform. S/he is not responsible for the validity of the design and analytic choices. All implementation steps are recorded and the implementation history is archived in the platform.

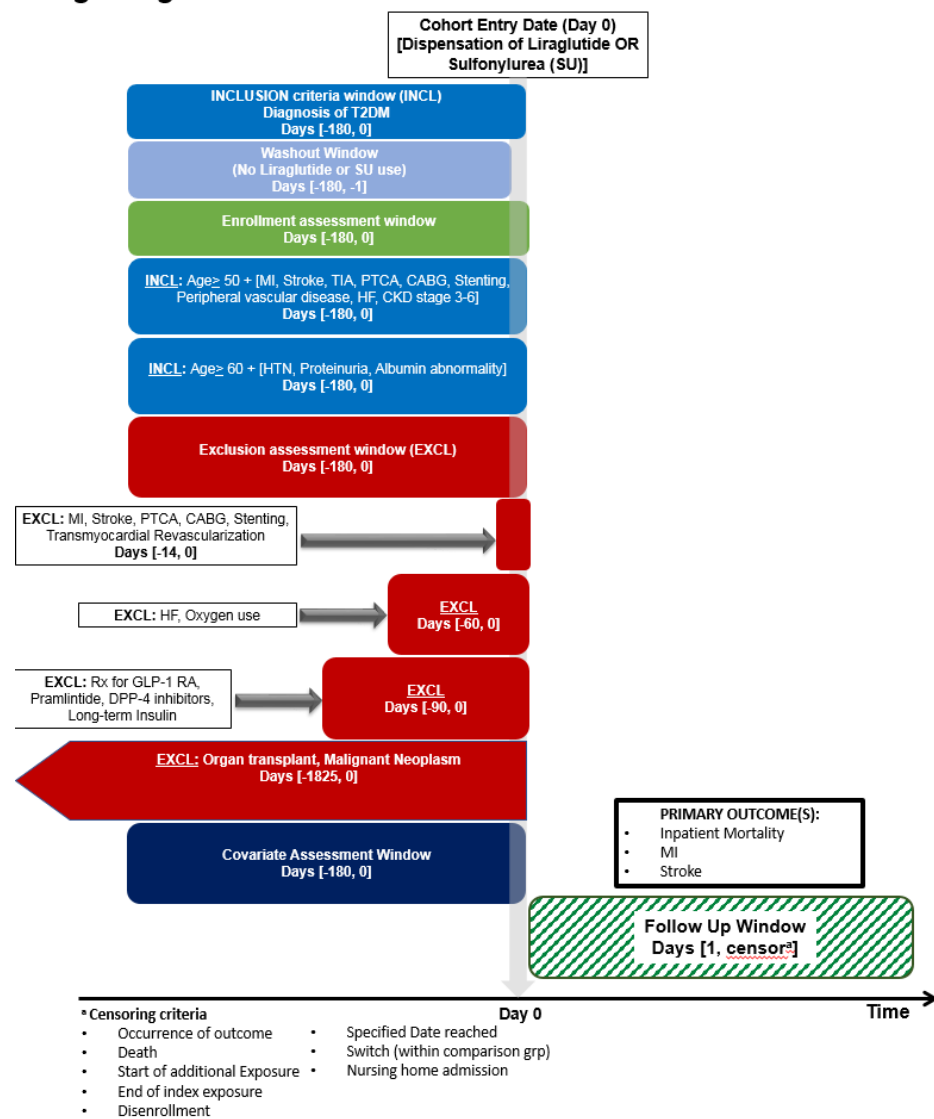
3. Data Source(s)

United/Optum, MarketScan, Medicare

4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.

Design Diagram – LEADER TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing liraglutide to the DPP4 inhibitor (DPP4i) antidiabetic class as a proxy for placebo. Both 2nd generation sulfonylureas (SUs) and DPP4is are not known to have an impact on the outcome of interest. The comparison against DPP4i is the **primary comparison**. Initiators of 2nd generation SUs are used as a secondary comparator group. The patients will be required to have continuous enrollment during the baseline period of 180 days before initiation of liraglutide or a comparator drug (cohort entry date). Follow-up for the outcome (3P-MACE), begins the day after drug initiation. As in the trial, patients are allowed to take other antidiabetic medications during the study.

5.2 Important steps for cohort formation

5.2.1 Eligible cohort entry dates

Market availability of liraglutide in the U.S. started on January 20, 2010.

- For Marketscan: January 20, 2010-Dec 31, 2017 (end of data availability).
- For Medicare: Jan 1, 2012-Dec 31, 2017 (start- end of data availability).
- For Optum: January 20, 2010-March 31, 2019 (end of data availability).

5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in **Appendix A** and are summarized in the flowcharts below.

5.3 Flowchart of the study cohort assembly

- For Liraglutide vs DPP4i

| | Optum | | Marketscan | | Medicare* | |
|--|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|
| | Less Excluded Patients | Remaining Patients | Less Excluded Patients | Remaining Patients | Less Excluded Patients | Remaining Patients |

Effectiveness research with Real World Data to support FDA's regulatory decision making: Protocol Template

| | | | | | | |
|---|-------------|------------|--------------|-------------|-------------|------------|
| All patients in the database | | 74,864,884 | | 191,990,035 | | 23,466,175 |
| Patients who used exposure or a reference between 20 January 2010 to Dec 2017 (for MarketScan)/March 2019 (for Optum) and 01 January 2012-December 2017 for Medicare | -74,012,464 | 852,420 | -190,638,745 | 1,351,290 | -21,492,649 | 1,973,526 |
| Patients who have continuous 6 months registration in the database | -111,929 | 740,491 | -134,586 | 1,216,704 | -516,146 | 1,457,380 |
| Patients without prior use of reference | -394,596 | 345,895 | -710,577 | 506,127 | -754,558 | 702,822 |
| Patients without prior use of exposure | -112,350 | 233,545 | -193,164 | 312,963 | -102,088 | 600,734 |
| Excluded because patient qualified in >1 exposure category | -75 | 233,470 | -138 | 312,825 | -48 | 600,686 |
| Patients who did not have missing age information | -10 | 233,460 | 0 | 312,825 | 0 | 600,686 |
| Patients who did not have missing gender information | -16 | 233,444 | 0 | 312,825 | 0 | 600,686 |
| Excluded based on Inclusion 1- DM Type 2 | -10,665 | 222,779 | -29,308 | 283,517 | -4,803 | 595,883 |
| Excluded based on Inclusion 3- Either Prior cardiovascular disease cohort or No Prior cardiovascular disease group | -42,768 | 180,011 | -98,418 | 185,099 | -17,351 | 578,532 |
| Excluded based on Exclusion 1- Type 1 diabetes | -3,952 | 176,059 | -4,538 | 180,561 | -14,315 | 564,217 |
| Excluded based on Exclusion 2- Use of GLP1 or Pramlintide or DPP4i within 3 months prior to index | -953 | 175,106 | -963 | 179,598 | -1,652 | 562,565 |
| Excluded based on Exclusion 3-Long Acting Insulin in prior 90 days | -7,143 | 167,963 | -5,629 | 173,969 | -21,421 | 541,144 |
| Excluded based on Exclusion 4-Diabetic ketoacidosis in prior 90 days | -112 | 167,851 | -84 | 173,885 | -359 | 540,785 |
| Excluded based on Exclusion 5- An acute coronary or cerebrovascular event in the previous 14 days | -546 | 167,305 | -720 | 173,165 | -1,764 | 539,021 |
| Excluded based on Exclusion 7- Oxygen canister use as a proxy for NYHA class IV | -286 | 167,019 | -297 | 172,868 | -1,919 | 537,102 |
| Excluded based on Exclusion 8- Current continuous renal replacement therapy/ESRD | -437 | 166,582 | -333 | 172,535 | -2,110 | 534,992 |
| Excluded based on Exclusion 10- Liver disease | -2,572 | 164,010 | -1,845 | 170,690 | -7,745 | 527,247 |
| Excluded based on Exclusion 11- Organ Transplant | -83 | 163,927 | -107 | 170,583 | -188 | 527,059 |
| Excluded based on Exclusion 12- History of Malignant Neoplasm in previous 5 years | -5,876 | 158,051 | -5,402 | 165,181 | -24,283 | 502,776 |
| Excluded based on Exclusion 13- Family or personal history of multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid carcinoma (FMTC) | -2 | 158,049 | -1 | 165,180 | -3 | 502,773 |
| Excluded based on Exclusion 14- Personal history of non-familial medullary thyroid carcinoma | 0 | 158,049 | 0 | 165,180 | 0 | 502,773 |

| | | | | | | |
|--|------|----------------|------|----------------|-------|----------------|
| Excluded based on Exclusion 17- Drug abuse or dependence | -450 | 157,599 | -164 | 165,016 | -878 | 501,895 |
| Excluded based on Exclusion 20- Contraception or pregnancy | -357 | 157,242 | -511 | 164,505 | -1002 | 500,893 |
| Final cohort | | 157,242 | | 164,505 | | 500,893 |

* Medicare database includes only patients with at least one diagnosis for diabetes, heart failure, or cerebrovascular disease.

• For Liraglutide vs 2nd Gen. SUs

| | Optum | | Marketscan | | Medicare* | |
|--|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|
| | Less Excluded Patients | Remaining Patients | Less Excluded Patients | Remaining Patients | Less Excluded Patients | Remaining Patients |
| All patients in the database | | 74,864,884 | | 191,990,035 | | 23,466,175 |
| Patients who used exposure or a reference between 20 January 2010 to Dec 2017 (for Marketscan)/March 2019 (for Optum) and 01 January 2012- December 2017 for Medicare | -73,337,305 | 1,527,579 | -189,889,741 | 2,100,294 | -19,968,954 | 3,497,221 |
| Patients who have continuous 6 months registration in the database | -204,156 | 1,323,423 | -233,189 | 1,867,105 | -952,050 | 2,545,171 |
| Patients without prior use of reference | -888,112 | 435,311 | -1,294,078 | 573,027 | -1,703,970 | 841,201 |
| Patients without prior use of exposure | -103,834 | 331,477 | -177,643 | 395,384 | -95,982 | 745,219 |
| Excluded because patient qualified in >1 exposure category | -138 | 331,339 | -236 | 395,148 | -85 | 745,134 |
| Patients who did not have missing age information | -14 | 331,325 | 0 | 395,148 | 0 | 745,134 |
| Patients who did not have missing gender information | -26 | 331,299 | 0 | 395,148 | 0 | 745,134 |
| Excluded based on Inclusion 1- DM Type 2 | -24,242 | 307,057 | -58,280 | 336,868 | -10,070 | 735,064 |
| Excluded based on Inclusion 3- Either Prior cardiovascular disease cohort or No Prior cardiovascular disease group | -62,008 | 245,049 | -130,017 | 206,851 | -24,553 | 710,511 |
| Excluded based on Exclusion 1- Type 1 diabetes | -4,763 | 240,286 | -5,243 | 201,608 | -15,909 | 694,602 |
| Excluded based on Exclusion 2- Use of GLP1 or Pramlintide or DPP4i within 3 months prior to index | -7,666 | 232,620 | -8,727 | 192,881 | -23,001 | 671,601 |
| Excluded based on Exclusion 3-Long Acting Insulin in prior 90 days | -6,604 | 226,016 | -5,151 | 187,730 | -19,399 | 652,202 |
| Excluded based on Exclusion 4-Diabetic ketoacidosis in prior 90 days | -169 | 225,847 | -151 | 187,579 | -442 | 651,760 |
| Excluded based on Exclusion 5- An acute coronary or cerebrovascular event in the previous 14 days | -806 | 225,041 | -1,218 | 186,361 | -2,112 | 649,648 |

| | | | | | | |
|---|--------|----------------|--------|----------------|---------|----------------|
| Excluded based on Exclusion 7- Oxygen canister use as a proxy for NYHA class IV | -3,508 | 221,533 | -2,257 | 184,104 | -3,451 | 646,197 |
| Excluded based on Exclusion 8- Current continuous renal replacement therapy/ESRD | -710 | 220,823 | -674 | 183,430 | -3,666 | 642,531 |
| Excluded based on Exclusion 10- Liver disease | -3,303 | 217,520 | -2,124 | 181,306 | -9,653 | 632,878 |
| Excluded based on Exclusion 11- Organ Transplant | -105 | 217,415 | -143 | 181,163 | -263 | 632,615 |
| Excluded based on Exclusion 12- History of Malignant Neoplasm in previous 5 years | -7,049 | 210,366 | -6,342 | 174,821 | -28,688 | 603,927 |
| Excluded based on Exclusion 13- Family or personal history of multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid carcinoma (FMTC) | -1 | 210,365 | 0 | 174,821 | -2 | 603,925 |
| Excluded based on Exclusion 14- Personal history of non-familial medullary thyroid carcinoma | 0 | 210,365 | 0 | 174,821 | 0 | 603,925 |
| Excluded based on Exclusion 17- Drug abuse or dependence | -638 | 209,727 | -226 | 174,595 | -1119 | 602,806 |
| Excluded based on Exclusion 20- Contraception or pregnancy | -371 | 209,356 | -453 | 174,142 | -967 | 601,839 |
| Final cohort | | 209,356 | | 174,142 | | 601,839 |

* Medicare database includes only patients with at least one diagnosis for diabetes, heart failure, or cerebrovascular disease.

6. Variables

6.1 Exposure-related variables:

Study drug:

The study exposure of interest is initiation of liraglutide. Initiation will be defined by no use of liraglutide or a comparator in the prior 6 months before treatment initiation (washout period).

Comparator agents:

- Initiators of liraglutide will be compared to initiators of-
 - DPP4i (**primary**)
 - 2nd generation sulfonylureas

Because liraglutide and comparators are frequently used as second or third line treatments of T2DM, we expect it to be unlikely that liraglutide and comparators are initiated in patients with substantially different baseline risk for proposed outcomes.

6.2 Preliminary covariates:

- Age
- Sex
- Combined Comorbidity Index (CCI), measured over the default baseline covariate assessment period, defined as 180 days prior to and including index date

Covariates listed above represent only a small subset of covariates that will ultimately be controlled for in the design and analysis. We use the covariates above only for initial feasibility analyses to judge whether there is likely to be sufficient overlap between treatment groups to proceed with the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and the initial power assessment and are listed in Table 1 (**Appendix B**). These covariates are based on those used by Patorno et al. (2019).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcomes of interest (definitions provided in **Appendix A**):

- **Primary outcome:** 3-point major adverse cardiovascular events (MACE), i.e., non-fatal myocardial infarction, non-fatal stroke, or CV mortality
- Secondary outcomes: Individual MACE components:
 - Hospital admission for MI (for purposes of individual component, fatal MI is included)
 - Hospital admission for stroke (for purposes of individual component, fatal stroke is included)
 - All-cause mortality/CV mortality:
 - All-cause inpatient mortality identified using discharge status codes will be used as a proxy for “CV mortality” in commercial databases
 - Information on CV mortality through data linkage with the National Death Index (NDI) will only become available at a later date for Medicare and will be used in secondary analyses.

Control outcomes of interest (control outcomes only serve to assess aspects of study validity but are not further interpreted):

1. For comparison with 2nd Gen. SUs: Severe hypoglycemia (we expect to see protective effect; American Diabetes Association, 2018)

Control outcome definitions

| Reference group | Outcome | Hospital Discharge Code(s) | Comments |
|--------------------------|---------------------|--|--|
| <i>Control Outcomes</i> | | | |
| 2 nd Gen. SUs | Severe hypoglycemia | <u>Severe hypoglycemia</u> Any-position ED or primary inpatient ICD-9 diagnosis: 251.0, 251.1x, 251.2x, or 250.8x. Outcomes identified by 250.8x are not included if they co-occur with one of the following diagnoses: 259.8, 272.7, 681.xx, 682.xx, 686.9, 707.1x, 707.2x, 707.8, 707.9, 709.3, 730.0x, 730.1x, 730.2x, 731.8 | <u>Note-</u> The corresponding ICD-10 codes will be used also |

6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analyses will be conducted with treatment defined as the index drug on the day of cohort entry. Because adherence in the real world databases is expected to be much worse than in the trial, the AT analysis is the **primary** analysis, as it targets the relative hazard of outcomes on treatment.

For the AT analyses, the follow-up will start the day after initiation of liraglutide and comparator and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest, unless otherwise specified for selected outcomes,
- The date of end of continuous registration in the database,
- End of the study period,
- Measured death event occurs,
- Nursing home admission
 - Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.

- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (liraglutide and comparator) plus a defined grace period (i.e., 60 days after the end of the last prescription's days' supply in main analyses).
- The date of augmentation or switching from an exposure to a comparator or any other agent in the comparator class and vice versa (e.g. switching from glimepiride to glipizide would be a censoring event);
 - A dosage change on the index treatment does not fulfill this criterion
 - An added treatment that is not part of the exposure or comparator group does not fulfill this criterion (e.g. if a liraglutide user adds insulin, he or she does not get censored at the time of insulin augmentation)

For the ITT analyses, the censoring based on the augmentation/switching and treatment discontinuation will be replaced with a maximum allowed follow-up time of 365 days.

7. Initial Feasibility Analysis

Action report links:

- For Liraglutide vs 2nd generation SUs

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/30594/result/0>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/30595/result/0>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/30593/result/0>

- For Liraglutide vs DPP4i

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/30606/result/0>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/30607/result/0>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/30605/result/0>

Date conducted: rerun on Jan 27, 2019

Complete Aetion feasibility analysis using age, sex, and CCI as the only covariates and the primary endpoint (Section 6.3.1) as the outcome. No measures of association will be computed nor will incidence rates stratified by treatment group.

- Report patient characteristics by treatment group

- Report summary parameters of the overall study population
- Report median follow-up time by treatment group
- Report reasons for censoring in the overall study population

8. Initial Power Assessment

Action report name:

- For Liraglutide vs 2nd SUs

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/30597/result/1>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/30596/result/1>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/30598/result/1>

- For Liraglutide vs DPP4i

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/30608/result/1>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/30609/result/1>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/30610/result/1>

Date conducted: rerun on Jan 27, 2019

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, sex, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

- Stop analyses until feasibility and power are reviewed by primary investigators and FDA. Reviewers evaluate the results of the analyses described above in Sections 7 and 8, including numbers of patients, patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power. These parameters are re-evaluated and reported in the subsequent sections, after incorporating feedback and refining the protocol.

| | | | |
|----------------------|---------------------|----------------|----------|
| Reviewed by PI: | Jessica M. Franklin | Date reviewed: | 10/26/18 |
| Reviewed by FDA: | David Martin | Date reviewed: | 1/10/19 |
| Reasons for stopping | | | |

| | |
|-------------------------|--|
| analysis (if required): | |
|-------------------------|--|

9. Balance Assessment after PS matching

Action report name:

- For Liraglutide vs 2nd Gen. SUs

Optum: <https://bwh-dope.aetion.com/projects/details/632/results/44783/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/633/results/45436/result/0>

Medicare: <https://bwh-dope.aetion.com/projects/details/634/results/45432/result/0>

- For Liraglutide vs DPP4i

Optum: <https://bwh-dope.aetion.com/projects/details/632/results/44786/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/633/results/44787/result/0>

Medicare: <https://bwh-dope.aetion.com/projects/details/634/results/45433/result/0>

Date conducted: 11/18/2019 (Medicare 11/30/2019)

After review of initial feasibility and power analyses, complete creation of the remaining covariates (see Table 1 below for list of covariates). Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates (excluding laboratory values, which are missing in some patients).

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

○ For Liraglutide vs DPP4i

| | Overall | Referent | Exposure |
|--|-----------------|-----------------|-----------------|
| Dummy Outcome | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |
| Death | 1,271 (0.75%) | 827 (0.98%) | 444 (0.53%) |
| Start of an additional exposure | 4,700 (2.79%) | 1,913 (2.27%) | 2,787 (3.30%) |
| End of index exposure | 99,981 (59.27%) | 45,078 (53.44%) | 54,903 (65.09%) |
| Specified date reached | 29,951 (17.76%) | 16,708 (19.81%) | 13,243 (15.70%) |
| End of patient enrollment | 22,798 (13.51%) | 12,483 (14.80%) | 10,315 (12.23%) |
| Switch to other SUs (for censoring) + nursing home admission | 9,989 (5.92%) | 7,336 (8.70%) | 2,653 (3.15%) |

○ For Liraglutide vs 2nd Gen. SUs

| | Overall | Referent | Exposure |
|--|-----------------|-----------------|-----------------|
| Dummy Outcome | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |
| Death | 858 (0.79%) | 595 (1.10%) | 263 (0.49%) |
| Start of an additional exposure | 4,294 (3.96%) | 967 (1.78%) | 3,327 (6.14%) |
| End of index exposure | 61,038 (56.33%) | 27,098 (50.01%) | 33,940 (62.64%) |
| Specified date reached | 21,830 (20.15%) | 13,222 (24.40%) | 8,608 (15.89%) |
| End of patient enrollment | 14,181 (13.09%) | 7,902 (14.58%) | 6,279 (11.59%) |
| Switch to other SUs (for censoring) + nursing home admission | 6,163 (5.69%) | 4,398 (8.12%) | 1,765 (3.26%) |

• Report follow-up time by treatment group.

○ For Liraglutide vs DPP4i

| | Median Follow-Up Time (Days) [IQR] | | |
|----------------------------|------------------------------------|---------------|---------------|
| Patient Group | Optum | Marketscan | Medicare |
| Overall Patient Population | 157 [88-334] | 185 [91-413] | 179 [92-381] |
| Referent | 173 [88-368] | 209 [112-437] | 209 [112-437] |
| Exposure | 148 [88-302] | 159 [88-331] | 159 [88-331] |

○ For Liraglutide vs 2nd Gen. SUs

| | Median Follow-Up Time (Days) [IQR] |
|--|------------------------------------|
|--|------------------------------------|

| Patient Group | Optum | Marketscan | Medicare |
|----------------------------|---------------|---------------|---------------|
| Overall Patient Population | 154 [88-339] | 168 [88-379] | 179 [98-397] |
| Referent | 181 [100-407] | 231 [128-500] | 231 [128-500] |
| Exposure | 148 [88-279] | 148 [88-307] | 148 [88-307] |

- Report risk per 1,000 patients

- For Liraglutide vs DPP4i

| | Optum | Marketscan | Medicare |
|-------------------------|-------|------------|----------|
| Risk per 1,000 patients | 14.30 | 12.11 | 38.60 |

- For Liraglutide vs 2nd Gen. SUs

| | Optum | Marketscan | Medicare |
|-------------------------|-------|------------|----------|
| Risk per 1,000 patients | 18.97 | 22.54 | 48.79 |

Action report name:

- For Liraglutide vs 2nd Gen. SUs

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/34412/result/0>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/34413/result/0>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/34414/result/0>

- For Liraglutide vs DPP4i

Optum: <https://bwh-dope.aetion.com/#/projects/details/632/results/34415/result/0>

Marketscan: <https://bwh-dope.aetion.com/#/projects/details/633/results/34416/result/0>

Medicare: <https://bwh-dope.aetion.com/#/projects/details/634/results/34417/result/0>

Date conducted: 04/25/2019

10. Final Power Assessment

Date conducted: 12/01/2019

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8. If the study is to be implemented in more than one database, copy and paste excel sheet to report power for each database separately and for the pooled analysis that uses data from all databases together. Power calculations are based on the formulas from Chow et al. (2008).

- For Liraglutide vs DPP4i

- Pooled

| Superiority Analysis | | Non-inferiority Analysis | |
|-----------------------------|-------------|---------------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 84,345 | Reference | 84,345 |
| Exposed | 84,345 | Exposed | 84,345 |
| Risk per 1,000 patients | 21.67 | Risk per 1,000 patients | 21.67 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 3655.5123 | Number of events expected | 3655.5123 |
| Power | 0.987775093 | Power | 0.999999999 |

- Optum

Effectiveness research with Real World Data to support FDA's regulatory decision making

| Superiority Analysis | | Non-inferiority Analysis | |
|-----------------------------|-------------|---------------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 19,187 | Reference | 19,187 |
| Exposed | 19,187 | Exposed | 19,187 |
| Risk per 1,000 patients | 14.30 | Risk per 1,000 patients | 14.30 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 548.7482 | Number of events expected | 548.7482 |
| Power | 0.371306397 | Power | 0.867151513 |

▪ Marketscan

| Superiority Analysis | | Non-inferiority Analysis | |
|-----------------------------|-------------|---------------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 20,777 | Reference | 20,777 |
| Exposed | 20,777 | Exposed | 20,777 |
| Risk per 1,000 patients | 12.11 | Risk per 1,000 patients | 12.11 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 503.21894 | Number of events expected | 503.21894 |
| Power | 0.345542948 | Power | 0.837143294 |

▪ Medicare

| Superiority Analysis | | Non-inferiority Analysis | |
|----------------------------|-------------|----------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 44,381 | Reference | 44,381 |
| Exposed | 44,381 | Exposed | 44,381 |
| Risk per 1,000 patients | 38.60 | Risk per 1,000 patients | 38.60 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 3426.2132 | Number of events expected | 3426.2132 |
| Power | 0.982819492 | Power | 0.999999995 |

○ For Liraglutide vs 2nd Gen. SUs

▪ Pooled

| Superiority Analysis | | Non-inferiority Analysis | |
|----------------------------|-------------|----------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 54,182 | Reference | 54,182 |
| Exposed | 54,182 | Exposed | 54,182 |
| Risk per 1,000 patients | 30.10 | Risk per 1,000 patients | 30.1 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 3261.7564 | Number of events expected | 3261.7564 |
| Power | 0.978141227 | Power | 0.999999984 |

▪ Optum

Effectiveness research with Real World Data to support FDA's regulatory decision making

| Superiority Analysis | | Non-inferiority Analysis | |
|----------------------------|-------------|----------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 12,253 | Reference | 12,253 |
| Exposed | 12,253 | Exposed | 12,253 |
| Risk per 1,000 patients | 18.97 | Risk per 1,000 patients | 18.97 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 464.87882 | Number of events expected | 464.87882 |
| Power | 0.323513047 | Power | 0.807428816 |

▪ Marketscan

| Superiority Analysis | | Non-inferiority Analysis | |
|----------------------------|-------------|----------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 13,591 | Reference | 13,591 |
| Exposed | 13,591 | Exposed | 13,591 |
| Risk per 1,000 patients | 22.54 | Risk per 1,000 patients | 22.54 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 612.68228 | Number of events expected | 612.68228 |
| Power | 0.406665538 | Power | 0.900972235 |

▪ Medicare

| Superiority Analysis | | Non-inferiority Analysis | |
|----------------------------|-------------|----------------------------|-------------|
| Number of patients matched | | Number of patients matched | |
| Reference | 28,338 | Reference | 28,338 |
| Exposed | 28,338 | Exposed | 28,338 |
| Risk per 1,000 patients | 48.79 | Risk per 1,000 patients | 48.79 |
| Desired HR from RCT | 0.87 | Assumed HR from RCT | 1 |
| Alpha (2-sided) | 0.05 | Alpha (2-sided) | 0.05 |
| | | Non-inferiority margin | 1.3 |
| | | | |
| Number of events expected | 2765.22204 | Number of events expected | 2765.22204 |
| Power | 0.955585785 | Power | 0.999999606 |

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board. Reviewers evaluate the results of the analyses described above in Sections 9 and 10, including numbers of patients, balance in patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power.

| | | | |
|--|------------------|----------------|----------|
| Reviewed by PI: | Jessica Franklin | Date reviewed: | 12/9/19 |
| Reviewed by FDA: | David Martin | Date reviewed: | 12/20/19 |
| Reasons for stopping analysis (if required): | | | |

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns: 12/20/19

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study

variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the individual respondent.

12. Register study protocol on clinicalTrials.gov

Date conducted:

- Register the study on [clinicalTrials.gov](https://clinicaltrials.gov) and upload this document.

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For **primary analysis**:

- In the PS-matched cohort from Section 9, calculate the HR for each outcome for liraglutide versus 2nd generation SU patients using a Cox proportional hazards model.

13.2 For secondary analyses:

- In the PS-matched cohort from Section 9, calculate the HR for each outcome for liraglutide versus DPP4i patients using a Cox proportional hazards model.
- In both pre-matched cohorts, perform asymmetrical trimming to remove patients with PS values below the 2.5th percentile of treated patients and above the 97.5th percentile of untreated patients. In the trimmed cohort, calculate the HR for canagliflozin versus referent patients using a Cox proportional hazards model, adjusting for deciles of the PS.

14. Requested Results

14.1 Results from primary and secondary analyses:

Separately for each endpoint and each comparator group:

| Analysis | No. exposed events | No. referent events | Exposed rate | Referent rate | HR (95% CI) |
|-------------------------|--------------------|---------------------|--------------|---------------|-------------|
| Crude | | | | | |
| Primary analysis | | | | | |
| Analysis 2 | | | | | |
| ... | | | | | |

HR, Hazard Ratio; CI, Confidence Interval.

15. References

American Diabetes Association. 8. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. 2018;41(Suppl 1):S73-S85. doi:10.2337/dc18-S008.

Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. **page 177**

Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM. Liraglutide and cardiovascular outcomes in type 2 diabetes. *New England Journal of Medicine*. 2016; 375(4):311-22.

Patorno E, Pawar A, Franklin JM, et al. Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study. *Circulation*. 2019; in press. (<https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.118.039177>)

Appendix A

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|---|--|--|---|--|
| # | LEADER trial definitions | Implementation in routine care | Please see the following Google Drive for further details or any missing information: https://drive.google.com/drive/folders/1WD618wrvwYiEaXfI_TcuK-V_Ccnb6h-gV2usp=sharing | |
| | Trial details- Secondary indication, 4a- unintended superiority with label change | | ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd-10-cm-and-pcs-crosswalk-general-equivalence-mapping.html | |
| | EXPOSURE vs. COMPARISON | | References/Rationale | Color coding |
| | Liraglutide versus placebo | Liraglutide vs. DPP4i or 2nd generation sulfonylurea | | Criteria |
| | PRIMARY OUTCOME | | | Adequate mapping in claims |
| | The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. HR=0.87 (95% CI 0.78-0.97) | Measured 1 days after drug initiation in diagnosis position specified below and inpatient care setting: Inpatient mortality/MI/Stroke -- For MI Any diagnosis position in inpatient care setting ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care), as the principal (primary) or the next (secondary) diagnosis For stroke Primary diagnosis position in inpatient care setting ICD-9 discharge diagnosis: 430.xx Subarachnoid hemorrhage (SAH) 431.xx Intracerebral hemorrhage (ICH) 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarction 434.xx (excluding 434.x0) Occlusion and stenosis of cerebral arteries with cerebral infarction 436.x Acute, but ill-defined cerebrovascular events Mortality- See Mortality Sheet. | For MI: →PPV 94% in Medicare claims data [Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. American heart journal 2004;148:99-104.] →PPV 88.4% in commercially-insured population [Wahl PM, Rodgers K, Schneeweiss S, et al. Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially-insured population. Pharmacoepidemiology and Drug Safety 2010;19:596-603.] For stroke: PPV of 85% or higher for ischemic stroke PPV ranging from 80% to 98% for hemorrhagic stroke →[Andrade SE, Harrold LR, Tjia J, et al. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. Pharmacoepidemiology and Drug Safety 2012;21 Suppl 1:100-28.] →[Tirschwell DL, Longstreth WT, Jr. Validating administrative data in stroke research. Stroke; a journal of cerebral circulation 2002;33:2465-70.] →[Roumie CL, Mitchell E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiology and drug safety 2008;17:20-6.] | Intermediate mapping in claims |
| | INCLUSION CRITERIA | | | Poor mapping or cannot be measured in claims |
| 1 | Men or women with type 2 diabetes | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting T2DM (ICD-9 Dx code of 250.x0 or 250.x2; ICD-10 Dx code of E11.x) | Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 | Can't be measured in claims but not important for the analysis |
| 2 | Anti-diabetic drug naïve or treated with one or more oral anti-diabetic drugs or treated with human NPH insulin or long-acting insulin analogue or premixed insulin, alone or in combination with OAD(s) | N/A (this is basically anyone) | | |
| 3 | Either of the following: • Prior cardiovascular disease: Age ≥ 50 years at screening, AND at least one of the following: o Prior MI o Prior stroke or TIA | Age ≥ 50 at drug initiation AND Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Acute MI: 410.xx, Old MI: 412.xx Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Stroke or TIA ICD-9 Dx: 430.xx, 431.xx, 433.xx, 434.xx, 435.xx, 436.xx | | |

Appendix A

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|----|--|---|--|
| 3a | | <p>Measured 180 days prior to drug initiation in any diagnosis position and care setting as defined below: Coronary revascularization (PTCA, stenting, CABG) PTCA: Inpatient CPT-4: 92973, 92982, 92984, 92995, 92996, 92920 – 92921, 92924 – 92925, 92937, 92938, 92941, 92943, 92944 OR – Inpatient or outpatient ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09</p> <p>Stenting: Inpatient CPT-4: 92980, 92981, 92928 – 92929, 92933 - 92934 OR – Inpatient or outpatient ICD-9 procedure: 36.06, 36.07</p> <p>CABG: Inpatient CPT-4: 33510 – 33536, 33545, 33572. OR – Inpatient or outpatient ICD-9 procedure: 36.1x, 36.2x</p> <p>Transmyocardial revascularization: Inpatient CPT-4: 33140, 33141 OR - Inpatient ICD-9 procedure: 36.31-36.34</p> | <p>Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p> |
| | o Prior coronary, carotid or peripheral arterial revascularization | | |
| | o >50% stenosis of coronary, carotid, or lower extremity arteries | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting 414.x, Peripheral vascular disease ICD9 diagnosis: 440.20 – 440.24, 440.29 – 440.32, 440.3, 440.4, 443.9</p> | <p>Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> |
| | o History of symptomatic CHD documented by positive exercise stress test or any cardiac imaging or unstable angina with ECG changes | N/A | |
| 3b | o Asymptomatic cardiac ischemia documented by positive nuclear imaging test, exercise test or dobutamine stress echo | N/A | |
| | o Chronic heart failure NYHA class II-III | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting ICD-9 diagnosis 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93</p> | <p>Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p> |
| | o Chronic renal failure: – eGFR <60 mL/min/1.73m2 (Modification of Diet in Renal Disease formula) | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting CKD stage 3-6 585.3x-585.6x</p> | |
| | – eGFR <60 mL/min (Cockcroft-Gault formula) | | |
| 4 | • No Prior cardiovascular disease: Age ≥ 60 years at screening, AND at least one of the following: | Age ≥ 60 at drug initiation AND | |
| | o Microalbuminuria or proteinuria | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Proteinuria ICD 9 DX 791.0 ICD10 DX R80.X Albumin abnormality ICD9 Dx- 790.99 ICD10 Dx - R77.0</p> | |
| | o Hypertension and left ventricular hypertrophy by ECG or imaging | <p>Measured 180 days prior to drug initiation in any diagnosis position and with 1 inpatient care setting claim AND 2 outpatient care setting claims: Hypertension any ICD-9 code from 401.x – 405.x</p> | <p>Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> |
| | o Left ventricular systolic or diastolic dysfunction by imaging | N/A | |
| 1 | o Ankle-brachial index <0.9 | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting ICD-9 440.21</p> | <p>Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p> |
| | HbA1c ≥ 7.0% at screening | N/A | |
| | EXCLUSION CRITERIA | | |
| | | | |
| 2 | Type 1 diabetes | <p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting DM type 1- At least 1 inpatient or outpatient ICD-9 Dx code of 250.x1 or 250.x3 or ICD-10 Dx code of E10.x in the 6 months prior to drug initiation.</p> | <p>Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p> |
| | Use of a GLP-1 receptor agonist (exenatide, liraglutide or other) or pramlintide or any (dipeptidyl peptidase 4 (DPP-4) inhibitor within the 3 months prior to screening | <p>Dispensing of at least one of the following medications in the 90 days prior to drug initiation: Use of a GLP-1 receptor agonist (exenatide, liraglutide or other) or pramlintide or any (dipeptidyl peptidase 4 (DPP-4) inhibitor within the 3 months prior to index date (Please see AHA therapy sheet.)</p> | |

Appendix A

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| 3 | Use of insulin other than human neutral protamine hagedorn (NPH) insulin or long-acting insulin analogue within 3 months prior to screening. Short-term use of other insulin during this period in connection with intercurrent illness is allowed at Investigator's discretion | Use of long-term insulin in 90 days prior to drug initiation defined as a claim for dispensing of insulin (Please see AHA therapy sheet for insulin). | |
| 4 | Acute decompensation of glycemic control requiring immediate intensification of treatment to prevent acute complications of diabetes (e.g., diabetic ketoacidosis) in the previous 3 months | Measured 90 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Diabetic ketoacidosis ICD-9 Diagnosis 250.1x | Bobo WV, Cooper WO, Epstein RA, Jr., Arbogast PG, Mounsey J, Ray WA. Positive predictive value of automated database records for diabetic ketoacidosis (DKA) in children and youth exposed to antipsychotic drugs or control medications: a Tennessee Medicaid Study. BMC medical research methodology 2011;11:157 Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |
| 5 | An acute coronary or cerebrovascular event in the previous 14 days | Measured 14 days prior to drug initiation in any diagnosis/procedure position and inpatient care setting MI, stroke, revascularization, PTCA, CABG: Acute MI ICD-9 diagnosis 410.xx Coronary revascularization- PTCA: Inpatient CPT-4: 92973, 92982, 92984, 92995, 92996, 92920 – 92921, 92924 – 92925, 92937, 92938, 92941, 92943, 92944 – OR – Inpatient ICD-9 procedure: 00.66, 36.01, 36.02, 36.03, 36.05, 36.09 Stenting: Inpatient CPT-4: 92980, 92981, 92928 – 92929, 92933 – 92934 – OR – Inpatient ICD-9 procedure: 36.06, 36.07 Transmyocardial revascularization CPT-4: 33140, 33141 – OR – Inpatient ICD-9 procedure: 36.31-36.34 CABG: Inpatient CPT-4: 33510 – 33536, 33545, 33572 – OR – Inpatient ICD-9 procedure: 36.1x, 36.2x Stroke ICD-9 diagnosis : 430.xx Subarachnoid hemorrhage (SAH) 431.xx Intracerebral hemorrhage (ICH) 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarction 434.x1 Occlusion and stenosis of cerebral arteries with cerebral infarction 436.x Acute, but ill-defined cerebrovascular events | |
| 6 | Currently planned coronary, carotid or peripheral artery revascularization | N/A | |
| 7 | Chronic heart failure NYHA class IV | Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient or outpatient care setting Oxygen use codes: HCPCS: E0424 E0425 E0430 E0431 E0433 E0434 E0435 E0439 E0440 E0441 E0442 E0443 E0444 E0447 E1390 E1391 E1392 E1405 E1406 K0738 S8120 S8121 or ICD-10 : Dependence on Supplemental oxygen Z99.81 ICD-9: Other dependence on machines, supplemental oxygen V46.2 | ORIGINAL DEFINITION: Inpatient Heart failure (CHF) in prior 60 days Any of ICD-9 codes: 428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93 NEW DEFINITION 4/22/2019: Inpatient diagnosis may not be specific enough for including severe symptomatic class IV patients. Therefore, we decided to incorporate the use of oxygen therapy (not limited to inpatient setting). |
| 8 | Current continuous renal replacement therapy | Measured 180 days prior to drug initiation in any procedure position and inpatient or outpatient care setting: ESRD (Please see ESRD codes tab for codes and algorithm used to define ESRD and Renal Transplant) | Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |
| 9 | Estimated glomerular filtration rate (eGFR) (as per MDRD) <30 mL/min/1.73m2 at screening. The criterion is applicable after a target number of 220 subjects with eGFR <30 mL/min are randomized | N/A | |
| 10 | End stage liver disease, defined as the presence of acute or chronic liver disease and recent history of one or more of the following: ascites, encephalopathy, variceal bleeding, bilirubin ≥ 2.0 mg/dL, albumin level ≤ 3.5 g/dL, prothrombin time ≥ 4 seconds prolonged, international normalized ratio (INR) ≥ 1.7 or prior liver transplant | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Liver disease- ICD-9 diagnosis: 070.xx, 570.xx- 573.xx 456.0x-456.2x, 576.8x, 782.4x, 789.5x ICD-9 procedure codes: 39.1x, 42.91 | Patorno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patorno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |

Appendix A

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| 11 | A prior solid organ transplant or awaiting solid organ transplant | Measured 180 days prior to drug initiation in any diagnosis/procedure position and inpatient or outpatient care setting Please see Organ transplant sheet for ICD-9 Diagnosis codes and ICD-9 and CPT procedure codes. | Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |
| 12 | Malignant neoplasm requiring chemotherapy, surgery, radiation or palliative therapy in the previous 5 years. Subjects with intraepithelial squamous cell carcinoma of the skin (Bowen's disease) treated with topical 5-fluorouracil (5FU) and subjects with basal cell skin cancer are allowed to enter the trial | Measured 1825 days prior to drug initiation in any procedure position and inpatient or outpatient care setting History of malignant neoplasm in previous 5 years 140.xx-208.xx (except 173.xx, non-melanoma skin cancer) | Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |
| 13 | Family or personal history of multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid carcinoma (FMTC) | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting ICD-9: MEN Type I: 258.01 MEN Type IIA: 258.02 MEN Type IIB: 258.03 ICD-10: MEN, unspecified: E31.20 MEN, Type I: E31.21 MEN Type IIA: E31.22 MEN, Type IIB: E31.23 | |
| 14 | Personal history of non-familial medullary thyroid carcinoma | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting: ICD9: 193 - MALIGNANT NEOPLASM OF THYROID GLAND 194.1 - MALIGNANT NEOPLASM OF PARATHYROID GLAND ICD10: C73 | (This is already covered in exclusion criteria #12, but measured and applied again) |
| 15 | Any acute condition or exacerbation of chronic condition that would in the Investigator's opinion interfere with the initial trial visit schedule and procedures | N/A | |
| 16 | Known or suspected hypersensitivity to trial product(s) or related products | N/A | |
| 17 | Known use of non prescribed narcotics or illicit drugs | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Drug abuse or dependence ICD-9: 292.xx, 304.xx, 305.2x-305.9x, 648.3x | Paterno, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Paterno, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177 |
| 18 | Simultaneous participation in any other clinical trial of an investigational agent. Participation in a clinical trial with investigational stent(s) is allowed | N/A | |
| 19 | Previous participation in this trial. Participation is defined as randomized | N/A | |
| 20 | Females of childbearing potential who are pregnant, breast-feeding or intend to become pregnant or are not using adequate contraceptive methods (adequate contraceptive measures as required by local law or practice) | Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting or any drug dispensing prior to drug initiation: i) Encounter for contraceptive management V25 OR Non-oral contraceptives (brand names)- Depo-subQ Provera 104 Depo-Provera, generic Mirena Ortho Evra NuvaRing Implanon Oral contraceptives (generic names)- See "oral contraceptives - generic" sheet. Oral contraceptives (brand names)- See "oral contraceptives iii) plus pregnancy Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting- Refer to Pregnancy Sheet. | Krumme, Alexis A. et. al. "Study protocol for the dabigatran, apixaban, rivaroxaban, edoxaban, warfarin comparative effectiveness research study." J. Comp. Eff. Res. (2018):7(1), 57-66. doi: 10.2217/cer-2017-0053. We excluded patients using contraceptives because this trial includes non-pregnant women, patients without childbearing potential, and patients who have childbearing potential but are taking precautions such as oral contraceptives (among many other ways) to avoid pregnancy during the trial period. It is impossible to implement such inclusion in real-world data, as childbearing potential is not recorded in claims. In this trials setting, this limitation to implement as an inclusion criteria is due to the following: i) lack of recording of contraceptives and other precautions to avoid pregnancy and ii) patients with diabetes and baseline CV tend to be older and are not likely to be at childbearing age. Therefore, we assumed that patients taking oral contraceptives have childbearing potential, so if they were to stop contraceptive use during follow-up, they could then become pregnant. Also, just to note, this exclusion of contraceptives use excludes very few patients (typically less than 0.1% of patients). |
| 21 | Receipt of any investigational medicinal product (IMP) within 30 days prior to this trial. | N/A | |

Appendix A

| | |
|---|---|
| <u>Trial ID</u> | |
| <u>Trial Name (with web links)</u> | LEADER |
| <u>Trial Name (with pdf links)</u> | |
| <u>NCT</u> | NCT01179048 |
| <u>Trial category</u> | Secondary indication |
| <u>Therapeutic Area</u> | Endocrinology |
| <u>RCT Category</u> | 4a- Unintended S with label change |
| <u>Brand Name</u> | |
| <u>Generic Name</u> | Liraglutide |
| <u>Sponsor</u> | Novo Nordisk A/S |
| <u>Year</u> | 2016 |
| <u>Measurable endpoint</u> | Composite of Cardiovascular Death, Non-fatal Myocardial Infarction, or Non-fatal Stroke |
| <u>Exposure</u> | Liraglutide |
| <u>Comparator</u> | Placebo |
| <u>Population</u> | |
| <u>Trial finding</u> | HR = 0.87 (95% CI 0.78-0.97) |
| <u>Notes</u> | |
| <u>No. of Patients</u> | |
| <u>Non-inferiority margin</u> | HR = 1.30 |
| <u>Assay Sens. Endpoint</u> | |
| <u>Assay Sens. Finding</u> | |
| <u>Power</u> | 90% power to detect non-inferiority |
| <u>Blinding</u> | |
| <u>Statistical Method</u> | |
| <u>Approval indication</u> | |

Appendix A

Mortality- Dependent on data source.

1. All-cause mortality / inpatient mortality

Identified using the vital status file-

Medicare

Identified using the discharge status codes-

Optum-

- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 27 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 28 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 29 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 40 = EXPIRED AT HOME (HOSPICE)
- 41 = EXPIRED IN A MEDICAL FACILITY (HOSPICE)
- 42 = EXPIRED - PLACE UNKNOWN (HOSPICE)

Truven-

- 20 - Died
- 22 - Died
- 23 - Died
- 24 - Died
- 25 - Died
- 26 - Died
- 27 - Died
- 28 - Died
- 29 - Died
- 40 - Other died status or Expired at home (Hospice claims only) (depends on year)

Appendix A

- 41 - Other died status or Expired in medical facility (Hospice claims only) (depends on year)
- 42 - Other died status or Expired - place unknown (Hospice claims only) (depends on year)
- 21 - Died or Disch./Transf. to court/law enforcement (depends on year)

2. CV mortality

Information on CV mortality through data linkage with the National Death Index (NDI) will be available for Medicare at a later date. We will conduct secondary analyses using CV mortality at that time.

Appendix A

| Antidiabetic class | Specific agent | Notes |
|--|--|--|
| SGLT2-inhibitors | Canagliflozin | Approved 3/29/2013 |
| | Dapagliflozin | |
| | Empagliflozin | |
| | Ertugliflozin | Approved Dec 21, 2017 |
| 2 nd generation sulfonylureas | Glimepiride | |
| | Glipizide | |
| | Glyburide | |
| DPP-4 inhibitors | Alogliptin | |
| | Linagliptin | |
| | Saxagliptin | |
| | Sitagliptin | |
| GLP-1 receptor agonist (GLP1-RA) | Exenatide | |
| | Liraglutide | |
| | Albiglutide | Approved April 15, 2014 and discontinued July 26, 2017 |
| | Dulaglutide | Approved Sep 18, 2014 |
| | Lixisenatide | Approved July 28, 2016 |
| | Semaglutide | Approved Dec 5, 2017 |
| Insulin | Insulin Aspart | |
| | Insulin Aspart/Insulin Aspart Protamine | |
| | Insulin Degludec | |
| | Insulin Detemir | |
| | Insulin Glargine | |
| | Insulin Glulisine | |
| | Insulin human isophane (NPH) | |
| | Insulin human regular (<i>search with NPH, don't want bf-pk</i>) | |
| | Insulin human regular/ Insulin human isophane (NPH) | |
| | Insulin Lispro | |
| | Insulin Lispro/Insulin Lispro Protamine | |
| Glitazones | Pioglitazone | |
| | Rosiglitazone | |

Appendix A

| | | |
|--|----------------|--|
| Meglitinides | Nateglinide | |
| | Repaglinide | |
| Alpha-glucosidase inhibitors | Acarbose | |
| | Miglitol | |
| Pramlintide | Pramlintide | |
| 1 st generation sulfonylureas | Acetohexamide | |
| | Chlorpropamide | |
| | Tolazamide | |
| | Tolbutamide | |

Appendix A

ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days

ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days

Codes include:

- ICD9 prox codes:

39.95, Hemodialysis

54.98, Peritoneal dialysis

- ICD9 dx codes:

585.5x, Chronic kidney disease, Stage V (for ESRD with no mention of dialysis)

585.6x, End stage renal disease (for ESRD with dialysis)

V56.0x, encounter for dialysis NOS

V56.8x, encounter for peritoneal dialysis

V45.1x, renal dialysis status

- CPT4 codes:

90957, 90960, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 4 or more face-to-face physician visits per month

90958, 90961, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 2-3 face-to-face physician visits per month

90959, 90962, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 1 face-to-face physician visit per month

90920, 90921, ESRD related services per full month; for patients 12-19 and twenty years of age and over

90924, 90925, ESRD related services (less than full month), per day; for patients 12-19 and twenty years of age and over

90935, Hemodialysis procedure with single physician evaluation

90937, Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription

90945, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single physician evaluation

90947, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated physician evaluations, with or without substantial revision of dialysis prescription

90965, 90966, ESRD related services for home dialysis per full month, for patients 12-19 and 20 years of age and older

90969, 90970, ESRD related services for dialysis less than a full month of service, per day; for patients 12-19 and 20 years of age and older

90989, Dialysis training, patient, including helper where applicable, any mode, completed course

90993, Dialysis training, patient, including helper where applicable, any mode, course not completed, per training session

90999, Unlisted dialysis procedure, inpatient or outpatient

99512, Home visit for hemodialysis

- HCPCS codes:

G0257, Unscheduled or emergency dialysis treatment for ESRD patient in a hospital outpatient dept. that is not certified as an ESRD facility

G0314, G0317, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/4 or more physician visit per month

Appendix A

G0315, G0318, ESRD related services during the course of treatment, for patients 12-19 and 20yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/2 or 3 physician visit per month

G0316, G0319, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/1 physician visit per month

G0322, G0323, ESRD related services for home dialysis patients per full month: for patients 12-19 and 20 yrs of age and over to include monitoring for adequacy of nutrition and etc.

G0326, G0327, ESRD related services for home dialysis (less than full month), per day; for patients 12-19 and 20 yrs of age and over

S9335, Home therapy, hemodialysis; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing services coded separately), per diem

S9339, Home therapy, peritoneal dialysis, administrative services, care coordination and all necessary supplies and equipment, per diem

OR

Kidney transplant, defined as either 1 inpatient or 1 outpatient code

Codes include:

-ICD9 dx codes:

V42.0x, Kidney transplant status

996.81 Complications of transplanted kidney

-ICD9 prox codes:

55.6x, Transplant of kidney (Exclude 55.61)

- CPT4 codes:

50360, Renal allotransplantation, implantation, graft, w/o donor & recipient nephrectomy

50365, Renal allotransplantation, implantation, graft, w/ donor & recipient nephrectomy

Appendix A

Organ Transplant

ICD-9 diagnoses:

V42.0 Kidney

V42.1 Heart

V42.6 Lung

V42.7 Liver

V42.8x Other specified organ or tissue

V42.81 Bone marrow

V42.83 Pancreas

V42.84 Intestines

V42.89 Other

V42.9x Unspecified organ or tissue

V58.44 Aftercare following organ transplant

E878.0x Surgical operation with transplant of whole organ

996.8x Complications of transplanted organ

ICD-9 procedures:

33.5x Lung transplant

33.6x Combined heart-lung transplantation

37.51 Heart transplantation

41.0x Bone marrow

46.97 Transplant of intestine

50.5x Liver transplant

52.8x Transplant of pancreas

55.6x Transplant of kidney

CPT4 codes

32851 LUNG TRANSPLANT, SINGLE; W/O CARDIOPULMONARY BYPASS

32852 LUNG TRANSPLANT, SINGLE; W/CARDIOPULMONARY BYPASS

32853 LUNG TRANSPLANT, DOUBLE (BILAT SEQUENTIAL/EN BLOC); W/O CARDIOPULMONARY BYPASS

32854 LUNG TRANSPLANT, DOUBLE (BILAT SEQUENTIAL/EN BLOC); W/CARDIOPULMONARY BYPASS

33935 HEART-LUNG TRANSPLANT W/RECIPIENT CARDIECTOMY-PNEUMONECTOMY

33945 HEART TRANSPLANT, W/WO RECIPIENT CARDIECTOMY

38240 BONE MARROW/BLOOD-DERIVED PERIPHERAL STEM CELL TRANSPLANTATION; ALLOGENIC

38241 BONE MARROW/BLOOD-DERIVED PERIPHERAL STEM CELL TRANSPLANTATION; AUTOLOGOUS

44135 INTESTINAL ALLOTRANSPLANTATION; FROM CADAVER DONOR

Appendix A

44136 INTESTINAL ALLOTRANSPLANTATION; FROM LIVING DONOR

47135 LIVER ALLOTRANSPLANTATION; ORTHOTOPIC, PARTIAL/WHOLE, FROM CADAVER/LIVING DONOR,
ANY AGE

47136 LIVER ALLOTRANSPLANTATION; HETEROTOPIC, PARTIAL/WHOLE, FROM CADAVER/LIVING DONOR,
ANY AGE

48554 TRANSPLANTATION, PANCREATIC ALLOGRAFT

48556 REMOVAL, TRANSPLANTED PANCREATIC ALLOGRAFT

50360 RENAL ALLOTRANSPLANTATION, IMPLANTATION, GRAFT; W/O DONOR & RECIPIENT NEPHRECTOMY

50365 RENAL ALLOTRANSPLANTATION, IMPLANTATION, GRAFT; W/RECIPIENT NEPHRECTOMY

50370 REMOVAL, TRANSPLANTED RENAL ALLOGRAFT

50380 RENAL AUTOTRANSPLANTATION, REIMPLANTATION, KIDNEY

Appendix A

| drug_class | Brand Name |
|--------------------|---------------|
| oral contraceptive | Apri; |
| oral contraceptive | Desogen; |
| oral contraceptive | Ortho-Cept; |
| oral contraceptive | Reclipsen |
| oral contraceptive | Kariva; |
| oral contraceptive | Mircette |
| oral contraceptive | Cyclessa; |
| oral contraceptive | Velivet |
| oral contraceptive | Yasmin |
| oral contraceptive | Yaz |
| oral contraceptive | Demulen 1/35; |
| oral contraceptive | Kelnor; |
| oral contraceptive | Zovia 1/25 |
| oral contraceptive | Demulen 1/50; |
| oral contraceptive | Zovia 1/50 |
| oral contraceptive | Alesse; |
| oral contraceptive | Aviane; |
| oral contraceptive | Lessina; |
| oral contraceptive | Lutera |
| oral contraceptive | Nordette; |
| oral contraceptive | Portia; |
| oral contraceptive | Levora |
| oral contraceptive | Lybrel |
| oral contraceptive | Seasonale; |
| oral contraceptive | Quasense; |
| oral contraceptive | Jolessa |
| oral contraceptive | Seasonique |
| oral contraceptive | Empresse; |
| oral contraceptive | Triphasil; |
| oral contraceptive | Trivora |
| oral contraceptive | Ovcon 35 |
| oral contraceptive | Balziva; |

Appendix A

| | |
|--------------------|----------------------|
| oral contraceptive | Femcon Fe |
| oral contraceptive | Brevicon; |
| oral contraceptive | Nortrel 0.5/35; |
| oral contraceptive | Modicon; |
| oral contraceptive | Necon 0.5/35 |
| oral contraceptive | Norinyl 1/35; |
| oral contraceptive | Nortrel 1/35; |
| oral contraceptive | Ortho-Novum 1/35; |
| oral contraceptive | Necon 1/35 |
| oral contraceptive | Ovcon 50; |
| oral contraceptive | Necon 1/50 |
| oral contraceptive | Ortho-Novum 10/11 |
| oral contraceptive | Aranelle; |
| oral contraceptive | Tri-Norinyl |
| oral contraceptive | Ortho-Novum 7/7/7; |
| oral contraceptive | Necon |
| oral contraceptive | Micronor; |
| oral contraceptive | Nor-QD; |
| oral contraceptive | Camila; |
| oral contraceptive | Errin; |
| oral contraceptive | Jolivet |
| oral contraceptive | Junel 21 1/20; |
| oral contraceptive | Junel 21 Fe 1/20; |
| oral contraceptive | Loestrin 21 1/20; |
| oral contraceptive | Loestrin 21 Fe 1/20; |
| oral contraceptive | Loestrin 24 Fe; |
| oral contraceptive | Microgestin 1/20 |
| oral contraceptive | Microgestin Fe 1/20 |
| oral contraceptive | Junel 21 1.5/30; |
| oral contraceptive | Junel 21 Fe 1.5/30; |
| oral contraceptive | Loestrin 1.5/30; |
| oral contraceptive | Loestrin Fe 1.5/30 |
| oral contraceptive | Microgestin 1.5/30 |

Appendix A

| | |
|--------------------|-----------------------|
| oral contraceptive | Microgestin Fe 1.5/30 |
| oral contraceptive | Ethrostep Fe; |
| oral contraceptive | Tilia Fe; |
| oral contraceptive | TriLegest Fe |
| oral contraceptive | Ortho-Cyclen; |
| oral contraceptive | Sprintec; |
| oral contraceptive | MonoNessa; |
| oral contraceptive | Previfem |
| oral contraceptive | Ortho Tri-Cyclen Lo; |
| oral contraceptive | Tri-Previfem; |
| oral contraceptive | TriNessa |
| oral contraceptive | Ortho Tri-Cyclen; |
| oral contraceptive | Tri-Sprintec |
| oral contraceptive | Cryselle; |
| oral contraceptive | Lo/Ovral; |
| oral contraceptive | Low-Ogestrel |
| oral contraceptive | Ovral; |
| oral contraceptive | Ogestrel |
| oral contraceptive | Zovia 1/50 |
| oral contraceptive | Alesse; |
| oral contraceptive | Aviane; |
| oral contraceptive | Lessina; |
| oral contraceptive | Lutera |
| oral contraceptive | Nordette; |
| oral contraceptive | Portia; |
| oral contraceptive | Levora |
| oral contraceptive | Lybrel |
| oral contraceptive | Seasonale; |
| oral contraceptive | Quasense; |
| oral contraceptive | Jolessa |
| oral contraceptive | Seasonique |
| oral contraceptive | Empresse; |
| oral contraceptive | Triphasil; |

Appendix A

| | |
|--------------------|----------------------|
| oral contraceptive | Trivora |
| oral contraceptive | Ovcon 35 |
| oral contraceptive | Balziva; |
| oral contraceptive | Femcon Fe |
| oral contraceptive | Brevicon; |
| oral contraceptive | Nortrel 0.5/35; |
| oral contraceptive | Modicon; |
| oral contraceptive | Necon 0.5/35 |
| oral contraceptive | Norinyl 1/35; |
| oral contraceptive | Nortrel 1/35; |
| oral contraceptive | Ortho-Novum 1/35; |
| oral contraceptive | Necon 1/35 |
| oral contraceptive | Ovcon 50; |
| oral contraceptive | Necon 1/50 |
| oral contraceptive | Ortho-Novum 10/11 |
| oral contraceptive | Aranelle; |
| oral contraceptive | Tri-Norinyl |
| oral contraceptive | Ortho-Novum 7/7/7; |
| oral contraceptive | Necon |
| oral contraceptive | Micronor; |
| oral contraceptive | Nor-QD; |
| oral contraceptive | Camila; |
| oral contraceptive | Errin; |
| oral contraceptive | Jolivette |
| oral contraceptive | Junel 21 1/20; |
| oral contraceptive | Junel 21 Fe 1/20; |
| oral contraceptive | Loestrin 21 1/20; |
| oral contraceptive | Loestrin 21 Fe 1/20; |
| oral contraceptive | Loestrin 24 Fe; |
| oral contraceptive | Microgestin 1/20 |
| oral contraceptive | Microgestin Fe 1/20 |
| oral contraceptive | Junel 21 1.5/30; |
| oral contraceptive | Junel 21 Fe 1.5/30; |

Appendix A

| | |
|--------------------|-----------------------|
| oral contraceptive | Loestrin 1.5/30; |
| oral contraceptive | Loestrin Fe 1.5/30 |
| oral contraceptive | Microgestin 1.5/30 |
| oral contraceptive | Microgestin Fe 1.5/30 |
| oral contraceptive | Estrostep Fe; |
| oral contraceptive | Tilia Fe; |
| oral contraceptive | TriLegest Fe |
| oral contraceptive | Ortho-Cyclen; |
| oral contraceptive | Sprintec; |
| oral contraceptive | MonoNessa; |
| oral contraceptive | Previfem |
| oral contraceptive | Ortho Tri-Cyclen Lo; |
| oral contraceptive | Tri-Previfem; |
| oral contraceptive | TriNessa |
| oral contraceptive | Ortho Tri-Cyclen; |
| oral contraceptive | Tri-Sprintec |
| oral contraceptive | Cryselle; |
| oral contraceptive | Lo/Ovral; |
| oral contraceptive | Low-Ogestrel |
| oral contraceptive | Ovral; |
| oral contraceptive | Ogestrel |

Appendix A

| drug_class | generic | generic_ndc |
|--------------------|-----------|--|
| oral contraceptive | estradiol | desogestrel-ethinyl estradiol |
| oral contraceptive | estradiol | desogestrel-ethinyl estradiol/ethinyl estradiol |
| oral contraceptive | estradiol | drospirenone/estradiol |
| oral contraceptive | estradiol | drospirenone/ethinyl estradiol/levomefolate calcium |
| oral contraceptive | estradiol | estradiol |
| oral contraceptive | estradiol | estradiol acetate |
| oral contraceptive | estradiol | estradiol benzoate |
| oral contraceptive | estradiol | estradiol cypionate |
| oral contraceptive | estradiol | estradiol cypionate/medroxyprogesterone acet |
| oral contraceptive | estradiol | estradiol hemihydrate, micronized |
| oral contraceptive | estradiol | estradiol micronized |
| oral contraceptive | estradiol | estradiol valerate |
| oral contraceptive | estradiol | estradiol valerate/dienogest |
| oral contraceptive | estradiol | estradiol valerate/sesame oil |
| oral contraceptive | estradiol | estradiol/estrone |
| oral contraceptive | estradiol | estradiol/estrone/vit b12 |
| oral contraceptive | estradiol | estradiol/levonorgestrel |
| oral contraceptive | estradiol | estradiol/norethindrone acetate |
| oral contraceptive | estradiol | estradiol/norgestimate |
| oral contraceptive | estradiol | estradiol/progesterone |
| oral contraceptive | estradiol | ethinyl estradiol |
| oral contraceptive | estradiol | ethinyl estradiol/drospirenone |
| oral contraceptive | estradiol | ethinyl estradiol/norethindrone acetate |
| oral contraceptive | estradiol | ethynodiol d-ethinyl estradiol |
| oral contraceptive | estradiol | ethynodiol diacetate-ethinyl estradiol |
| oral contraceptive | estradiol | etonogestrel/ethinyl estradiol |
| oral contraceptive | estradiol | levonorgestrel-ethinyl estradiol |
| oral contraceptive | estradiol | levonorgestrel/ethinyl estradiol and ethinyl estradiol |
| oral contraceptive | estradiol | me-testosterone/eth estradiol |
| oral contraceptive | estradiol | metttrm/estradiol/multivits |
| oral contraceptive | estradiol | norelgestromin/ethinyl estradiol |
| oral contraceptive | estradiol | norethindrone a-e estradiol |

Appendix A

| | | |
|--------------------|----------------|--|
| oral contraceptive | estradiol | norethindrone a-e estradiol/fe |
| oral contraceptive | estradiol | norethindrone a-e estradiol/ferrous fumarate |
| oral contraceptive | estradiol | norethindrone acetate-ethinyl estradiol |
| oral contraceptive | estradiol | norethindrone acetate-ethinyl estradiol/ferrous fumarate |
| oral contraceptive | estradiol | norethindrone-ethin estradiol |
| oral contraceptive | estradiol | norethindrone-ethinyl estradiol |
| oral contraceptive | estradiol | norethindrone-ethinyl estradiol/ferrous fumarate |
| oral contraceptive | estradiol | norgestimate-ethinyl estradiol |
| oral contraceptive | estradiol | norgestrel-ethinyl estradiol |
| oral contraceptive | estradiol | testosterone cypionate/estradiol cypionate |
| oral contraceptive | estradiol | testosterone enanthate/estradiol valerate |
| oral contraceptive | estradiol | testosterone/estradiol |
| oral contraceptive | levonorgestrel | estradiol/levonorgestrel |
| oral contraceptive | levonorgestrel | levonorgestrel |
| oral contraceptive | levonorgestrel | levonorgestrel-eth estra |
| oral contraceptive | levonorgestrel | levonorgestrel-eth estra/pregnancy test kit |
| oral contraceptive | levonorgestrel | levonorgestrel-ethinyl estradiol |
| oral contraceptive | levonorgestrel | levonorgestrel/ethinyl estradiol and ethinyl estradiol |
| oral contraceptive | norethindrone | estradiol/norethindrone acetate |
| oral contraceptive | norethindrone | ethinyl estradiol/norethindrone acetate |
| oral contraceptive | norethindrone | leuprolide acetate/norethindrone acetate |
| oral contraceptive | norethindrone | norethindrone |
| oral contraceptive | norethindrone | norethindrone a-e estradiol |
| oral contraceptive | norethindrone | norethindrone a-e estradiol/fe |
| oral contraceptive | norethindrone | norethindrone a-e estradiol/ferrous fumarate |
| oral contraceptive | norethindrone | norethindrone acetate |
| oral contraceptive | norethindrone | norethindrone acetate-ethinyl estradiol |
| oral contraceptive | norethindrone | norethindrone acetate-ethinyl estradiol/ferrous fumarate |
| oral contraceptive | norethindrone | norethindrone-ethin estradiol |
| oral contraceptive | norethindrone | norethindrone-ethinyl estrad |
| oral contraceptive | norethindrone | norethindrone-ethinyl estradiol |
| oral contraceptive | norethindrone | norethindrone-ethinyl estradiol/ferrous fumarate |

Appendix A

| | | |
|--------------------|-------------------------|------------------------------|
| oral contraceptive | norethindrone | norethindrone-mestranol |
| oral contraceptive | norgestrel | norgestrel |
| oral contraceptive | norgestrel | norgestrel-ethinyl estradiol |
| oral contraceptive | polyestradiol phosphate | polyestradiol phosphate |

Appendix A

Pregnancy

Dx codes

650 NORMAL DELIVERY
660 OBSTRUCTED LABOR
661 ABNORMALITY OF FORCES OF LABOR
662 LONG LABOR
663 UMBILICAL CORD COMPLICATIONS DURING LABOR AND DELIVERY
664 TRAUMA TO PERINEUM AND VULVA DURING DELIVERY
665 OTHER OBSTETRICAL TRAUMA
667 RETAINED PLACENTA OR MEMBRANES WITHOUT HEMORRHAGE
668 COMPLICATIONS OF THE ADMINISTRATION OF ANESTHETIC OR OTHER SEDATION IN LABOR AND DELIVERY
669.94 UNSPECIFIED COMPLICATION OF LABOR AND DELIVERY POSTPARTUM CONDITION OR COMPLICATION
V24 POSTPARTUM CARE AND EXAMINATION
V24.0 POSTPARTUM CARE AND EXAMINATION IMMEDIATELY AFTER DELIVERY
V24.1 POSTPARTUM CARE AND EXAMINATION OF LACTATING MOTHER
V24.2 ROUTINE POSTPARTUM FOLLOW
V27 OUTCOME OF DELIVERY
V27.0 MOTHER WITH SINGLE LIVEBORN
V27.1 MOTHER WITH SINGLE STILLBORN
V27.2 MOTHER WITH TWINS BOTH LIVEBORN
V27.3 MOTHER WITH TWINS ONE LIVEBORN AND ONE STILLBORN
V27.4 MOTHER WITH TWINS BOTH STILLBORN
V27.5 MOTHER WITH OTHER MULTIPLE BIRTH ALL LIVEBORN
V27.6 MOTHER WITH OTHER MULTIPLE BIRTH SOME LIVEBORN
V27.7 MOTHER WITH OTHER MULTIPLE BIRTH ALL STILLBORN
V27.9 MOTHER WITH UNSPECIFIED OUTCOME OF DELIVERY

Procedure codes

72.0 LOW FORCEPS OPERATION
72.1 LOW FORCEPS OPERATION WITH EPISIOTOMY
72.2 MID FORCEPS OPERATION
72.21 MID FORCEPS OPERATION WITH EPISIOTOMY
72.29 OTHER MID FORCEPS OPERATION
72.3 HIGH FORCEPS OPERATION
72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
72.39 OTHER HIGH FORCEPS OPERATION

Appendix A

72.00 OTHER NON-INSTRUMENTAL DELIVERY

72.4 FORCEPS ROTATION OF FETAL HEAD

72.5 BREECH EXTRACTION

72.51 PARTIAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD

72.52 OTHER PARTIAL BREECH EXTRACTION

72.53 TOTAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD

72.54 OTHER TOTAL BREECH EXTRACTION

72.6 FORCEPS APPLICATION TO AFTERCOMING HEAD

72.7 VACUUM EXTRACTION

72.71 VACUUM EXTRACTION WITH EPISIOTOMY

72.79 OTHER VACUUM EXTRACTION

72.8 OTHER SPECIFIED INSTRUMENTAL DELIVERY

72.9 UNSPECIFIED INSTRUMENTAL DELIVERY

73.0 ARTIFICIAL RUPTURE OF MEMBRANES

73.01 INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF MEMBRANES

73.09 OTHER ARTIFICIAL RUPTURE OF MEMBRANES

73.1 OTHER SURGICAL INDUCTION OF LABOR

73.2 INTERNAL AND COMBINED VERSION AND EXTRACTION

73.21 INTERNAL AND COMBINED VERSION WITHOUT EXTRACTION

73.22 INTERNAL AND COMBINED VERSION WITH EXTRACTION

73.3 FAILED FORCEPS

73.4 MEDICAL INDUCTION OF LABOR

73.5 MANUALLY ASSISTED DELIVERY

73.51 MANUAL ROTATION OF FETAL HEAD

73.59 OTHER MANUALLY ASSISTED DELIVERY

73.6 EPISIOTOMY

73.8 OPERATIONS ON FETUS TO FACILITATE DELIVERY

73.9 OTHER OPERATIONS ASSISTING DELIVERY

73.91 EXTERNAL VERSION ASSISTING DELIVERY

73.92 REPLACEMENT OF PROLAPSED UMBILICAL CORD

73.93 INCISION OF CERVIX TO ASSIST DELIVERY

73.94 PUBIOTOMY TO ASSIST DELIVERY

73.99 OTHER OPERATIONS ASSISTING DELIVERY

74.0 CLASSICAL CESAREAN SECTION

74.1 LOW CERVICAL CESAREAN SECTION

74.2 EXTRAPERITONEAL CESAREAN SECTION

Appendix A

74.02 EXTRATUBAL PREGNANCY, UNSPECIFIED TYPE

74.3 REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY

74.4 CESAREAN SECTION OF OTHER SPECIFIED TYPE

74.9 CESAREAN SECTION OF UNSPECIFIED TYPE

74.91 HYSTEROTOMY TO TERMINATE PREGNANCY

74.99 OTHER CESAREAN SECTION OF UNSPECIFIED TYPE

75.4 MANUAL REMOVAL OF RETAINED PLACENTA

75.5 REPAIR OF CURRENT OBSTETRIC LACERATION OF UTERUS

75.6 REPAIR OF OTHER CURRENT OBSTETRIC LACERATION

75.7 MANUAL EXPLORATION OF UTERINE CAVITY, POSTPARTUM

75.9 OTHER OBSTETRIC OPERATIONS

Appendix B: Liraglutide vs DPP4i

Optum

MarketScan

Medicare

BEFORE PS MATCHING

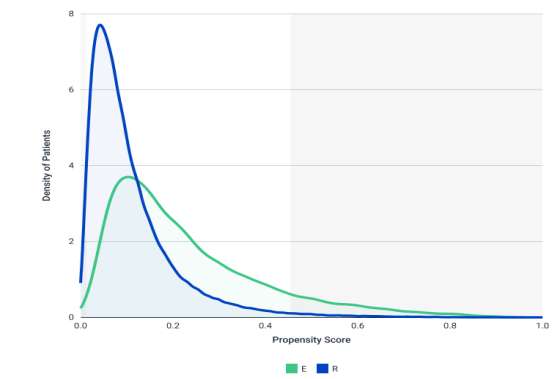


Figure 49: Pre-matching propensity score overlap

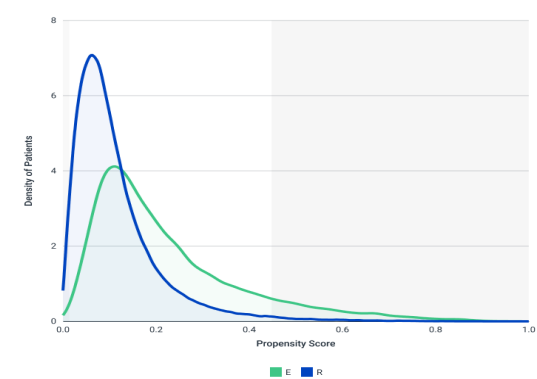


Figure 49: Pre-matching propensity score overlap

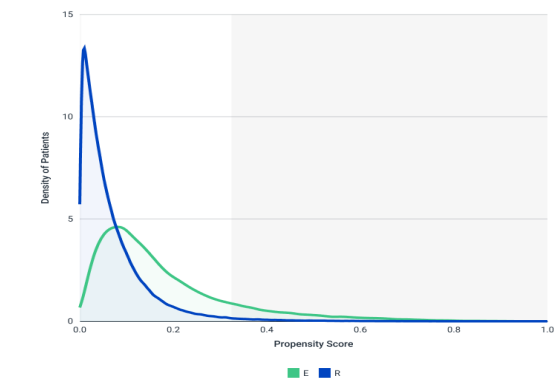


Figure 25: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.763. The post-matching c-statistic was 0.528.

The c-statistics for the propensity score model, pre-matching was 0.749. The post-matching c-statistic was 0.523.

The c-statistics for the propensity score model, pre-matching was 0.788. The post-matching c-statistic was 0.52.

AFTER PS MATCHING

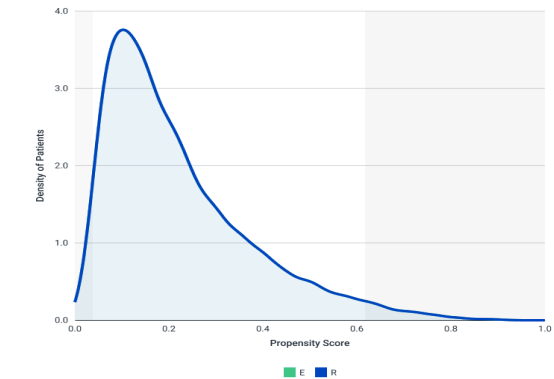


Figure 50: Post-matching propensity score overlap

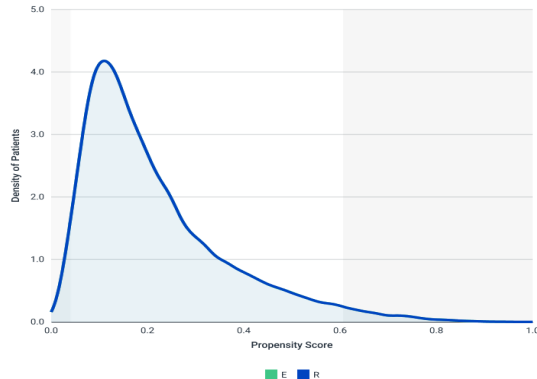


Figure 50: Post-matching propensity score overlap

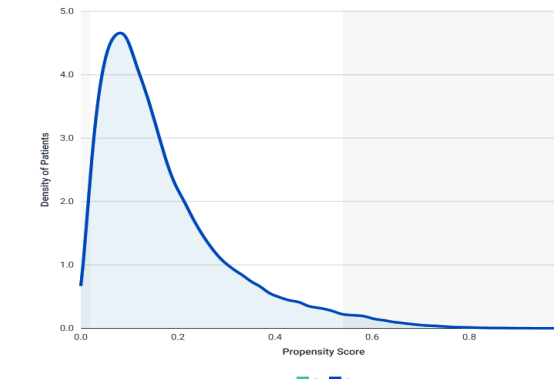


Figure 26: Post-matching propensity score overlap

Table 1: Liraglutide vs DPP4i

| Unmatched | | | | | | | | | | | |
|---|----------------------|-----------------------|-----------|----------------------|-----------------------|-----------|----------------------|-----------------------|-----------|------------------|-----------|
| Variable | Optum | | | MarketScan | | | Medicare | | | POOLED | |
| | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | St. Diff. |
| Number of patients | 137,649 | 19,460 | | 143,337 | 21,041 | | 454,700 | 44,778 | | 735,686 | |
| Age | | | | | | | | | | | |
| ...mean (sd) | 70.07 (8.03) | 66.00 (6.84) | 0.55 | 66.74 (8.79) | 63.07 (6.32) | 0.48 | 74.48 (7.29) | 70.59 (5.00) | 0.62 | 72.15 (7.74) | 0.65 |
| ...median [IQR] | 69.00 [65.00, 76.00] | 66.00 [61.00, 70.00] | 0.40 | 64.00 [61.00, 72.00] | 62.00 [60.00, 66.00] | 0.26 | 73.00 [69.00, 79.00] | 70.00 [67.00, 73.00] | 0.64 | 70.50 (7.74) | 0.57 |
| Age categories | | | | | | | | | | | |
| ...18 - 54; n (%) | 3,645 (2.6%) | 1,088 (5.6%) | -0.15 | 7,490 (5.2%) | 1,773 (8.4%) | -0.13 | 0 (0.0%) | 0 (0.0%) | #DIV/0! | 11,135 (1.5%) | -0.12 |
| ...55 - 64; n (%) | 30,092 (21.9%) | 6,913 (35.5%) | -0.30 | 68,184 (47.6%) | 12,865 (61.1%) | -0.27 | 7,142 (1.6%) | 1,114 (2.5%) | -0.06 | 105,418 (14.3%) | -0.26 |
| ...65 - 74; n (%) | 64,422 (46.8%) | 9,363 (48.1%) | -0.03 | 39,328 (27.4%) | 5,193 (24.7%) | 0.06 | 250,319 (55.1%) | 34,945 (78.0%) | -0.50 | 354,069 (48.1%) | -0.20 |
| ...≥ 75; n (%) | 39,490 (28.7%) | 2,096 (10.8%) | 0.46 | 28,335 (19.8%) | 1,210 (5.8%) | 0.43 | 197,239 (43.4%) | 8,719 (19.5%) | 0.53 | 265,064 (36.0%) | 0.52 |
| Gender - United | | | | | | | | | | | |
| ...Males; n (%) | 68,305 (49.6%) | 9,191 (47.2%) | 0.05 | 80,527 (56.2%) | 10,789 (51.3%) | 0.10 | 197,449 (43.4%) | 19,778 (44.2%) | -0.02 | 346,281 (47.1%) | 0.01 |
| ...Females; n (%) | 69,344 (50.4%) | 10,269 (52.8%) | -0.05 | 62,810 (43.8%) | 10,252 (48.7%) | -0.10 | 257,251 (56.6%) | 25,000 (55.8%) | 0.02 | 389,405 (52.9%) | -0.01 |
| Race | | | | | | | | | | | |
| ...White; n (%) | N/A | N/A | | N/A | N/A | | 337,843 (74.3%) | 38,225 (85.4%) | -0.28 | 337,843 (74.3%) | -0.28 |
| ...Black; n (%) | N/A | N/A | | N/A | N/A | | 52,880 (11.6%) | 3,806 (8.5%) | 0.10 | 52,880 (11.6%) | 0.10 |
| ...Asian; n (%) | N/A | N/A | | N/A | N/A | | 23,337 (5.1%) | 531 (1.2%) | 0.22 | 23,337 (5.1%) | 0.22 |
| ...Hispanic; n (%) | N/A | N/A | | N/A | N/A | | 21,402 (4.7%) | 801 (1.8%) | 0.16 | 21,402 (4.7%) | 0.16 |
| ...North American Native; n (%) | N/A | N/A | | N/A | N/A | | 2,392 (0.5%) | 177 (0.4%) | 0.01 | 2,392 (0.5%) | 0.01 |
| ...Other/Unknown; n (%) | N/A | N/A | | N/A | N/A | | 16,846 (3.7%) | 1,238 (2.8%) | 0.05 | 16,846 (3.7%) | 0.05 |
| Region - United (umping missing&other category with West) | | | | | | | | | | | |
| ...Northeast; n (%) | 17,444 (12.7%) | 1,756 (9.0%) | 0.12 | 32,182 (22.5%) | 3,998 (19.0%) | 0.09 | 90,962 (20.0%) | 7,000 (15.6%) | 0.12 | 140,588 (19.1%) | 0.11 |
| ...South; n (%) | 67,640 (49.1%) | 10,375 (53.3%) | -0.08 | 34,576 (24.1%) | 4,549 (21.6%) | 0.06 | 193,181 (42.5%) | 20,663 (46.1%) | -0.07 | 295,397 (40.2%) | -0.03 |
| ...Midwest; n (%) | 23,768 (17.3%) | 3,839 (19.7%) | -0.06 | 59,121 (41.2%) | 9,927 (47.2%) | -0.12 | 92,885 (20.4%) | 10,345 (23.1%) | -0.07 | 175,774 (23.9%) | -0.10 |
| ...West; n (%) | 28,797 (20.9%) | 3,490 (17.9%) | 0.08 | 16,027 (11.2%) | 2,339 (11.1%) | 0.00 | 77,672 (17.1%) | 6,770 (15.1%) | 0.05 | 122,496 (16.7%) | 0.05 |
| ...Unknown+missing; n (%) | N/A | N/A | #VALUE! | 1,431 (1.0%) | 228 (1.1%) | -0.01 | N/A | N/A | #VALUE! | 1,431 (1.0%) | -0.01 |
| CV Covariates | | | | | | | | | | | |
| Ischemic heart disease; n (%) | 39,052 (28.4%) | 5,847 (30.0%) | | 46,475 (32.4%) | 6,900 (32.8%) | | 148,750 (32.7%) | 13,938 (31.1%) | | 234,277 (31.8%) | 0.01 |
| Acute MI; n (%) | 2,315 (1.7%) | 293 (1.5%) | | 2,658 (1.9%) | 311 (1.5%) | | 8,356 (1.8%) | 541 (1.2%) | | 13,329 (1.8%) | 0.04 |
| ACS/unstable angina; n (%) | 2,694 (2.0%) | 397 (2.0%) | | 3,152 (2.2%) | 438 (2.1%) | | 9,368 (2.1%) | 748 (1.7%) | | 15,214 (2.1%) | 0.01 |
| Old MI; n (%) | 5,390 (3.9%) | 786 (4.0%) | | 3,482 (2.4%) | 438 (2.1%) | | 19,366 (4.3%) | 1,616 (3.6%) | | 28,430 (3.8%) | 0.03 |
| Stable angina; n (%) | 5,780 (4.2%) | 956 (4.9%) | | 4,996 (3.5%) | 757 (3.6%) | | 18,469 (4.1%) | 1,724 (3.9%) | | 29,245 (4.0%) | 0.00 |
| Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%) | 36,533 (26.5%) | 5,496 (28.2%) | | 44,110 (30.8%) | 6,595 (31.3%) | | 141,426 (31.1%) | 13,340 (29.8%) | | 222,069 (30.2%) | 0.01 |
| Other atherosclerosis with ICD10 ; n (%) | 1,696 (1.2%) | 203 (1.0%) | | 2,017 (1.4%) | 9,310 (2.0%) | | 241 (0.0%) | 763 (1.7%) | | 1,207 (0.0%) | 0.03 |
| Previous cardiac procedure (CABG or PTCA or Stent) ; n (%) | 1,201 (0.9%) | 173 (0.9%) | | 1,786 (1.2%) | 215 (1.0%) | | 3,709 (0.8%) | 238 (0.5%) | | 6,696 (0.9%) | 0.02 |
| History of CABG or PTCA; n (%) | 9,173 (6.7%) | 1,426 (7.3%) | | 5,910 (4.1%) | 847 (4.0%) | | 40,580 (8.9%) | 3,742 (8.4%) | | 55,663 (7.6%) | 0.02 |
| Any stroke; n (%) | 11,660 (8.5%) | 1,418 (7.3%) | | 13,094 (9.1%) | 1,523 (7.2%) | | 50,128 (11.0%) | 3,815 (8.5%) | | 74,882 (10.2%) | 0.08 |
| Ischemic stroke (w and w/o mention of cerebral infarction); n (%) | 11,493 (8.3%) | 1,407 (7.2%) | | 12,931 (9.0%) | 1,502 (7.1%) | | 49,540 (10.9%) | 3,782 (8.4%) | | 73,964 (10.1%) | 0.08 |
| Hemorrhagic stroke; n (%) | 380 (0.3%) | 31 (0.2%) | | 374 (0.3%) | 36 (0.2%) | | 1,464 (0.3%) | 62 (0.1%) | | 2,218 (0.3%) | 0.02 |
| TIA; n (%) | 2,932 (2.1%) | 331 (1.7%) | | 3,274 (2.3%) | 368 (1.7%) | | 11,914 (2.6%) | 775 (1.7%) | | 18,120 (2.5%) | 0.06 |
| Other cerebrovascular disease; n (%) | 3,355 (2.4%) | 336 (1.7%) | | 2,664 (1.9%) | 239 (1.1%) | | 15,532 (3.4%) | 900 (2.0%) | | 21,551 (2.9%) | 0.08 |
| Late effects of cerebrovascular disease; n (%) | 3,094 (2.2%) | 249 (1.3%) | | 2,107 (1.5%) | 151 (0.7%) | | 13,901 (3.1%) | 635 (1.4%) | | 19,102 (2.6%) | 0.10 |
| Cerebrovascular procedure; n (%) | 152 (0.1%) | 21 (0.1%) | | 223 (0.2%) | 24 (0.1%) | | 649 (0.1%) | 45 (0.1%) | | 1,024 (0.1%) | 0.00 |
| Heart failure (CHF); n (%) | 15,587 (11.3%) | 2,094 (10.8%) | | 13,361 (9.3%) | 1,604 (7.6%) | | 66,067 (14.5%) | 4,972 (11.1%) | | 95,015 (12.9%) | 0.08 |
| Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%) | 13,999 (10.2%) | 1,740 (8.9%) | | 12,644 (8.8%) | 1,696 (8.1%) | | 61,829 (13.6%) | 4,595 (10.3%) | | 88,472 (12.0%) | 0.08 |
| Atrial fibrillation; n (%) | 12,890 (9.4%) | 1,576 (8.1%) | | 11,832 (8.3%) | 1,252 (6.0%) | | 61,761 (13.6%) | 4,822 (10.8%) | | 86,483 (11.8%) | 0.09 |
| Other cardiac dysrhythmia; n (%) | 15,067 (10.9%) | 2,040 (10.5%) | | 12,311 (8.6%) | 1,494 (7.1%) | | 65,098 (14.3%) | 5,160 (11.5%) | | 92,476 (12.6%) | 0.08 |
| Cardiac conduction disorders; n (%) | 4,626 (3.4%) | 552 (2.8%) | | 3,820 (2.7%) | 436 (2.1%) | | 21,875 (4.8%) | 1,645 (3.7%) | | 30,321 (4.1%) | 0.05 |
| Other CVD; n (%) | 18,872 (13.7%) | 2,321 (11.9%) | | 18,649 (13.0%) | 2,291 (10.9%) | | 80,263 (17.7%) | 6,364 (14.2%) | | 117,784 (16.0%) | 0.09 |
| Diabetes-related complications | | | | | | | | | | | |
| Diabetic retinopathy; n (%) | 9,042 (6.6%) | 1,525 (7.8%) | | 6,336 (4.4%) | 1,047 (5.0%) | | 31,125 (6.8%) | 3,764 (8.4%) | | 46,503 (6.3%) | -0.04 |
| Diabetes with other ophthalmic manifestations; n (%) | 1,130 (0.8%) | 141 (0.7%) | | 4,518 (3.2%) | 737 (3.5%) | | 12,856 (2.8%) | 1,482 (3.3%) | | 18,504 (2.5%) | -0.02 |
| Retinal detachment, vitreous hemorrhage, vitrectomy; n (%) | 545 (0.4%) | 86 (0.4%) | | 493 (0.3%) | 72 (0.3%) | | 1,742 (0.4%) | 199 (0.4%) | | 2,780 (0.4%) | 0.00 |
| Retinal laser coagulation therapy; n (%) | 788 (0.6%) | 123 (0.6%) | | 860 (0.6%) | 140 (0.7%) | | 2,635 (0.6%) | 299 (0.7%) | | 4,283 (0.6%) | -0.01 |
| Occurrence of Diabetic Neuropathy ; n (%) | 26,233 (19.1%) | 4,774 (24.5%) | | 16,101 (11.2%) | 3,065 (14.6%) | | 85,054 (18.7%) | 10,489 (23.4%) | | 127,388 (17.3%) | -0.11 |
| Occurrence of diabetic nephropathy with ICD10 ; n (%) | 24,423 (17.7%) | 3,525 (18.1%) | | 10,351 (7.2%) | 1,700 (8.1%) | | 51,602 (11.3%) | 5,673 (12.7%) | | 86,376 (11.7%) | -0.03 |
| Hypoglycemia ; n (%) | 4,226 (3.1%) | 479 (2.5%) | | 4,131 (2.9%) | 640 (3.0%) | | 16,613 (3.7%) | 1,391 (3.1%) | | 24,970 (3.4%) | 0.03 |
| Hyperglycemia; n (%) | 5,948 (4.3%) | 763 (3.9%) | | 4,259 (3.0%) | 551 (2.6%) | | 22,441 (4.9%) | 1,684 (3.8%) | | 32,648 (4.4%) | 0.05 |
| Disorders of fluid electrolyte and acid-base balance; n (%) | 13,161 (9.6%) | 1,370 (7.0%) | | 9,325 (6.5%) | 966 (4.6%) | | 54,745 (12.0%) | 3,370 (7.5%) | | 77,231 (10.5%) | 0.14 |
| Diabetic ketoacidosis; n (%) | 154 (0.1%) | 21 (0.1%) | | 131 (0.1%) | 23 (0.1%) | | 600 (0.1%) | 53 (0.1%) | | 885 (0.1%) | 0.00 |
| Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%) | 771 (0.6%) | 97 (0.5%) | | 554 (0.4%) | 74 (0.4%) | | 2,583 (0.6%) | 198 (0.4%) | | 3,908 (0.5%) | 0.01 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | |
|---|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|---------|
| Diabetes with peripheral circulatory disorders with ICD-10 ; n (%) | 11,656 (8.5%) | 1,552 (8.0%) | 6,329 (4.4%) | 895 (4.3%) | 37,479 (8.2%) | 3,252 (7.3%) | 55,464 (7.5%) | 5,699 (6.7%) | 0.03 |
| Diabetic Foot; n (%) | 3,308 (2.4%) | 511 (2.6%) | 3,247 (2.3%) | 499 (2.4%) | 14,118 (3.1%) | 1,392 (3.1%) | 20,673 (2.8%) | 2,402 (2.8%) | 0.00 |
| Gangrene; n (%) | 454 (0.3%) | 52 (0.3%) | 349 (0.2%) | 34 (0.2%) | 1,484 (0.3%) | 86 (0.2%) | 2,287 (0.3%) | 172 (0.2%) | 0.02 |
| Lower extremity amputation; n (%) | 902 (0.7%) | 151 (0.8%) | 457 (0.3%) | 72 (0.3%) | 3,083 (0.7%) | 234 (0.5%) | 4,442 (0.6%) | 457 (0.5%) | 0.01 |
| Osteomyelitis; n (%) | 868 (0.6%) | 113 (0.6%) | 820 (0.6%) | 123 (0.6%) | 3,123 (0.7%) | 230 (0.5%) | 4,811 (0.7%) | 466 (0.5%) | 0.03 |
| Skin infections; n (%) | 7,852 (5.7%) | 1,189 (6.1%) | 8,388 (5.9%) | 1,314 (6.2%) | 34,416 (7.6%) | 3,405 (7.6%) | 50,656 (6.9%) | 5,908 (6.9%) | 0.00 |
| Erectile dysfunction; n (%) | 3,529 (2.6%) | 598 (3.1%) | 3,240 (2.3%) | 533 (2.5%) | 9,341 (2.1%) | 1,329 (3.0%) | 16,110 (2.2%) | 2,460 (2.9%) | -0.04 |
| Diabetes with unspecified complication; n (%) | 7,318 (5.3%) | 1,250 (6.4%) | 5,581 (3.9%) | 1,021 (4.9%) | 22,683 (5.0%) | 2,517 (5.6%) | 35,582 (4.8%) | 4,788 (5.6%) | -0.04 |
| Diabetes mellitus without mention of complications; n (%) | 123,499 (89.7%) | 16,933 (87.0%) | 135,666 (94.6%) | 19,693 (93.6%) | 431,062 (94.8%) | 41,725 (93.2%) | 690,227 (93.8%) | 78,351 (91.9%) | 0.07 |
| Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%) | 131,194 (95.3%) | 18,548 (95.3%) | 126,524 (88.3%) | 18,623 (88.5%) | 440,639 (96.9%) | 43,436 (97.0%) | 698,357 (94.9%) | 80,607 (94.5%) | 0.02 |
| Hyperlipidemia; n (%) | 107,176 (77.9%) | 15,367 (79.0%) | 96,564 (67.4%) | 14,951 (71.1%) | 366,495 (80.6%) | 37,204 (83.1%) | 570,235 (77.5%) | 67,522 (79.2%) | -0.04 |
| Edema; n (%) | 11,564 (8.4%) | 1,754 (9.0%) | 8,574 (6.0%) | 1,320 (6.3%) | 51,918 (11.4%) | 4,855 (10.8%) | 72,056 (9.8%) | 7,929 (9.3%) | 0.02 |
| Renal Dysfunction (non-diabetic) ; n (%) | 38,064 (27.7%) | 4,698 (24.1%) | 25,130 (17.5%) | 3,050 (14.5%) | 122,954 (27.0%) | 10,060 (22.5%) | 186,148 (25.3%) | 17,808 (20.9%) | 0.10 |
| Occurrence of acute renal disease ; n (%) | 7,144 (5.2%) | 626 (3.2%) | 5,405 (3.8%) | 390 (1.9%) | 29,118 (6.4%) | 1,432 (3.2%) | 41,667 (5.7%) | 2,448 (2.9%) | 0.14 |
| Occurrence of chronic renal insufficiency; n (%) | 32,496 (23.6%) | 4,049 (20.8%) | 18,932 (13.2%) | 2,380 (11.3%) | 103,426 (22.7%) | 8,660 (19.3%) | 154,854 (21.0%) | 15,089 (17.7%) | 0.08 |
| Chronic kidney disease ; n (%) | 31,532 (22.9%) | 3,938 (20.2%) | 18,355 (12.8%) | 2,295 (10.9%) | 98,398 (21.6%) | 8,194 (18.3%) | 148,285 (20.2%) | 14,427 (16.9%) | 0.08 |
| CKD Stage 3-4; n (%) | 22,711 (16.5%) | 2,899 (14.9%) | 13,419 (9.4%) | 1,727 (8.2%) | 69,048 (15.2%) | 5,916 (13.2%) | 105,178 (14.3%) | 10,542 (12.4%) | 0.06 |
| Occurrence of hypertensive nephropathy; n (%) | 14,200 (10.3%) | 1,746 (9.0%) | 7,062 (4.9%) | 877 (4.2%) | 48,654 (10.7%) | 3,522 (7.9%) | 69,916 (9.5%) | 6,145 (7.2%) | 0.08 |
| Occurrence of miscellaneous renal insufficiency ; n (%) | 9,326 (6.8%) | 1,025 (5.3%) | 7,297 (5.1%) | 794 (3.8%) | 39,407 (8.7%) | 2,911 (6.5%) | 56,030 (7.6%) | 4,730 (5.5%) | 0.08 |
| Glaucoma or cataracts ; n (%) | 31,519 (22.9%) | 4,099 (21.1%) | 27,054 (18.9%) | 3,736 (17.8%) | 125,334 (27.6%) | 12,591 (28.1%) | 183,907 (25.0%) | 20,426 (24.0%) | 0.02 |
| Cellulitis or abscess of toe; n (%) | 1,938 (1.4%) | 309 (1.6%) | 1,442 (1.0%) | 215 (1.0%) | 7,035 (1.5%) | 672 (1.5%) | 10,415 (1.4%) | 1,196 (1.4%) | 0.00 |
| Foot ulcer; n (%) | 3,246 (2.4%) | 492 (2.5%) | 3,305 (2.3%) | 501 (2.4%) | 14,168 (3.1%) | 1,370 (3.1%) | 20,719 (2.8%) | 2,363 (2.8%) | 0.00 |
| Bladder stones; n (%) | 206 (0.1%) | 14 (0.1%) | 179 (0.1%) | 22 (0.1%) | 782 (0.2%) | 73 (0.2%) | 1,167 (0.2%) | 109 (0.1%) | 0.03 |
| Kidney stones; n (%) | 3,106 (2.3%) | 470 (2.4%) | 3,373 (2.4%) | 521 (2.5%) | 12,208 (2.7%) | 1,306 (2.9%) | 18,687 (2.5%) | 2,297 (2.7%) | -0.01 |
| Urinary tract infections (UTIs); n (%) | 14,737 (10.7%) | 1,747 (9.0%) | 10,494 (7.3%) | 1,378 (6.5%) | 72,585 (16.0%) | 5,522 (12.3%) | 97,816 (13.3%) | 8,647 (10.1%) | 0.10 |
| Dipstick urinalysis; n (%) | 53,139 (38.6%) | 7,035 (36.2%) | 46,136 (32.2%) | 6,828 (32.5%) | 195,617 (43.0%) | 17,919 (40.0%) | 294,892 (40.1%) | 31,782 (37.3%) | 0.06 |
| Non-dipstick urinalysis; n (%) | 59,310 (43.1%) | 8,756 (45.0%) | 43,231 (30.2%) | 7,574 (36.0%) | 186,851 (41.1%) | 20,869 (46.6%) | 289,392 (39.3%) | 37,199 (43.6%) | -0.09 |
| Urine function test; n (%) | 3,515 (2.6%) | 470 (2.4%) | 3,953 (2.8%) | 508 (2.4%) | 15,791 (3.5%) | 1,537 (3.4%) | 23,259 (3.2%) | 2,515 (2.9%) | 0.02 |
| Cytology; n (%) | 1,262 (0.9%) | 129 (0.7%) | 1,590 (1.1%) | 181 (0.9%) | 5,167 (1.1%) | 408 (0.9%) | 8,019 (1.1%) | 718 (0.8%) | 0.03 |
| Cysts; n (%) | 1,614 (1.2%) | 241 (1.2%) | 1,968 (1.4%) | 261 (1.2%) | 6,557 (1.4%) | 662 (1.5%) | 10,139 (1.4%) | 1,164 (1.4%) | 0.00 |
| Other Covariates | | | | | | | | | |
| Liver disease; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | #VALUE! | 000 (0.0%) | #VALUE! |
| Osteoarthritis; n (%) | 24,718 (18.0%) | 3,864 (19.9%) | 19,572 (13.7%) | 3,249 (15.4%) | 113,591 (25.0%) | 11,128 (24.9%) | 157,881 (21.5%) | 18,241 (21.4%) | 0.00 |
| Other arthritis, arthropathies and musculoskeletal pain; n (%) | 51,843 (37.7%) | 7,843 (40.3%) | 48,371 (33.7%) | 7,762 (36.9%) | 213,921 (47.0%) | 21,204 (47.4%) | 314,135 (42.7%) | 36,809 (43.2%) | -0.01 |
| Dorsopathies; n (%) | 29,810 (21.7%) | 5,119 (26.3%) | 26,948 (18.8%) | 4,549 (21.6%) | 122,994 (27.0%) | 13,499 (30.1%) | 179,752 (24.4%) | 23,167 (27.2%) | -0.06 |
| Fractures; n (%) | 4,494 (3.3%) | 551 (2.8%) | 4,287 (3.0%) | 536 (2.5%) | 20,423 (4.5%) | 1,579 (3.5%) | 29,204 (4.0%) | 2,666 (3.1%) | 0.05 |
| Falls ; n (%) | 5,598 (4.1%) | 619 (3.2%) | 1,915 (1.3%) | 186 (0.9%) | 24,100 (5.3%) | 1,497 (3.3%) | 31,613 (4.3%) | 2,302 (2.7%) | 0.09 |
| Osteoporosis; n (%) | 8,985 (6.5%) | 791 (4.1%) | 5,336 (3.7%) | 613 (2.9%) | 45,290 (10.0%) | 2,896 (6.5%) | 59,611 (8.1%) | 4,300 (5.0%) | 0.13 |
| Hyperthyroidism; n (%) | 1,099 (0.8%) | 129 (0.7%) | 819 (0.6%) | 109 (0.5%) | 4,909 (1.1%) | 417 (0.9%) | 6,827 (0.9%) | 655 (0.8%) | 0.01 |
| Hypothyroidism; n (%) | 22,924 (16.7%) | 3,807 (19.6%) | 16,633 (11.6%) | 3,024 (14.4%) | 73,337 (16.1%) | 7,801 (17.4%) | 112,894 (15.3%) | 14,632 (17.2%) | -0.05 |
| Other disorders of thyroid gland ; n (%) | 5,049 (3.7%) | 994 (5.1%) | 4,703 (3.3%) | 1,015 (4.8%) | 20,113 (4.4%) | 2,618 (5.8%) | 29,865 (4.1%) | 4,627 (5.4%) | -0.06 |
| Depression; n (%) | 11,373 (8.3%) | 2,024 (10.4%) | 8,745 (6.1%) | 1,648 (7.8%) | 52,459 (11.5%) | 5,355 (12.0%) | 72,577 (9.9%) | 9,027 (10.6%) | -0.02 |
| Anxiety; n (%) | 9,539 (6.9%) | 1,739 (8.9%) | 6,316 (4.4%) | 1,089 (5.2%) | 40,669 (8.9%) | 3,761 (8.4%) | 56,524 (7.7%) | 6,589 (7.7%) | 0.00 |
| Sleep_Disorder; n (%) | 9,838 (7.1%) | 2,106 (10.8%) | 14,014 (9.8%) | 3,538 (16.8%) | 39,861 (8.8%) | 5,970 (13.3%) | 63,713 (8.7%) | 11,614 (13.6%) | -0.16 |
| Dementia; n (%) | 7,136 (5.2%) | 406 (2.1%) | 4,259 (3.0%) | 213 (1.0%) | 43,046 (9.5%) | 1,485 (3.3%) | 54,441 (7.4%) | 2,104 (2.5%) | 0.23 |
| Delirium; n (%) | 2,267 (1.6%) | 146 (0.8%) | 1,699 (1.2%) | 93 (0.4%) | 13,093 (2.9%) | 487 (1.1%) | 17,059 (2.3%) | 726 (0.9%) | 0.11 |
| Psychosis; n (%) | 1,770 (1.3%) | 132 (0.7%) | 1,328 (0.9%) | 80 (0.4%) | 12,498 (2.7%) | 410 (0.9%) | 15,596 (2.1%) | 622 (0.7%) | 0.12 |
| Obesity; n (%) | 24,341 (17.7%) | 6,527 (33.5%) | 16,530 (11.5%) | 4,589 (21.8%) | 63,591 (14.0%) | 11,795 (26.3%) | 104,462 (14.2%) | 22,911 (26.9%) | -0.32 |
| Overweight; n (%) | 7,251 (5.3%) | 839 (4.3%) | 2,562 (1.8%) | 362 (1.7%) | 15,407 (3.4%) | 1,228 (2.7%) | 25,220 (3.4%) | 2,429 (2.8%) | 0.03 |
| Smoking; n (%) | 14,135 (10.3%) | 2,261 (11.6%) | 7,307 (5.1%) | 980 (4.7%) | 55,934 (12.3%) | 5,420 (12.1%) | 77,376 (10.5%) | 8,661 (10.2%) | 0.01 |
| Alcohol abuse or dependence; n (%) | 870 (0.6%) | 86 (0.4%) | 555 (0.4%) | 59 (0.3%) | 2,506 (0.6%) | 159 (0.4%) | 3,931 (0.5%) | 304 (0.4%) | 0.01 |
| Drug abuse or dependence; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | #VALUE! | 00 (0.0%) | #VALUE! |
| COPD; n (%) | 14,198 (10.3%) | 1,973 (10.1%) | 10,318 (7.2%) | 1,275 (6.1%) | 56,882 (12.5%) | 4,948 (11.1%) | 81,398 (11.1%) | 8,196 (9.6%) | 0.05 |
| Asthma; n (%) | 7,979 (5.8%) | 1,423 (7.3%) | 6,641 (4.6%) | 1,245 (5.9%) | 30,514 (6.7%) | 3,532 (7.9%) | 45,134 (6.1%) | 6,200 (7.3%) | -0.05 |
| Obstructive sleep apnea; n (%) | 11,663 (8.5%) | 3,609 (18.5%) | 13,366 (9.3%) | 3,712 (17.6%) | 29,991 (6.6%) | 6,268 (14.0%) | 55,020 (7.5%) | 13,589 (15.9%) | -0.26 |
| Pneumonia; n (%) | 4,591 (3.3%) | 441 (2.3%) | 4,180 (2.9%) | 411 (2.0%) | 20,756 (4.6%) | 1,181 (2.6%) | 29,527 (4.0%) | 2,033 (2.4%) | 0.09 |
| Imaging; n (%) | 241 (0.2%) | 26 (0.1%) | 159 (0.1%) | 15 (0.1%) | 1,166 (0.3%) | 50 (0.1%) | 1,566 (0.2%) | 91 (0.1%) | 0.03 |
| Diabetes Medications | | | | | | | | | |
| DM Medications - AGIs; n (%) | 786 (0.6%) | 99 (0.5%) | 633 (0.4%) | 81 (0.4%) | 2,985 (0.7%) | 256 (0.6%) | 4,404 (0.6%) | 436 (0.5%) | 0.01 |
| DM Medications - Glitazones; n (%) | 16,871 (12.3%) | 2,269 (11.7%) | 22,209 (15.5%) | 3,302 (15.7%) | 45,631 (10.0%) | 4,744 (10.6%) | 84,711 (11.5%) | 10,315 (12.1%) | -0.02 |
| DM Medications - Insulin; n (%) | 8,831 (6.4%) | 3,535 (18.2%) | 8,235 (5.7%) | 3,628 (17.2%) | 34,893 (7.7%) | 8,976 (20.0%) | 51,959 (7.1%) | 16,139 (18.9%) | -0.36 |
| DM Medications - Meglitinides; n (%) | 1,810 (1.3%) | 216 (1.1%) | 2,892 (2.0%) | 362 (1.7%) | 9,363 (2.1%) | 694 (1.5%) | 14,065 (1.9%) | 1,272 (1.5%) | 0.03 |
| DM Medications - Metformin; n (%) | 96,324 (70.0%) | 12,338 (63.4%) | 102,745 (71.7%) | 13,977 (66.4%) | 309,951 (68.2%) | 29,057 (64.9%) | 509,020 (69.2%) | 55,372 (64.9%) | 0.09 |
| Concomitant initiation or current use of SGLT2i; n (%) | 3,835 (2.8%) | 1,082 (5.6%) | 3,828 (2.7%) | 1,012 (4.8%) | 7,655 (1.7%) | 1,707 (3.8%) | 15,318 (2.1%) | 3,801 (4.5%) | -0.13 |
| Concomitant initiation or current use of AGIs; n (%) | 545 (0.4%) | 67 (0.3%) | 447 (0.3%) | 48 (0.2%) | 2,115 (0.5%) | 174 (0.4%) | 3,107 (0.4%) | 289 (0.3%) | 0.02 |
| Concomitant initiation or current use of Glitazones; n (%) | 10,920 (7.9%) | 1,656 (8.5%) | 14,399 (10.0%) | 2,407 (11.4%) | 30,752 (6.8%) | 3,542 (7.9%) | 56,071 (7.6%) | 7,605 (8.9%) | -0.05 |
| Concomitant initiation or current use of 2nd Generation SUs; n (%) | 51,739 (37.6%) | 5,743 (29.5%) | 49,362 (34.4%) | 6,207 (29.5%) | 174,253 (38.3%) | 14,795 (33.0%) | 275,354 (37.4%) | 26,745 (31.4%) | 0.13 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | |
|---|----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|---------|
| Concomitant initiation or current use of Insulin; n (%) | 4,972 (3.6%) | 2,133 (11.0%) | 4,622 (3.2%) | 2,182 (10.4%) | 19,944 (4.4%) | 5,427 (12.1%) | 29,538 (4.0%) | 9,742 (11.4%) | -0.28 |
| Concomitant initiation or current use of Meglitinides; n (%) | 1,297 (0.9%) | 137 (0.7%) | 2,114 (1.5%) | 252 (1.2%) | 6,897 (1.5%) | 472 (1.1%) | 10,308 (1.4%) | 861 (1.0%) | 0.04 |
| Concomitant initiation or current use of Metformin; n (%) | 81,351 (59.1%) | 10,014 (51.5%) | 87,805 (61.3%) | 11,257 (53.5%) | 260,323 (57.3%) | 23,718 (53.0%) | 429,479 (58.4%) | 44,989 (52.8%) | 0.11 |
| Past use of SGLT2i ; n (%) | 1,518 (1.1%) | 416 (2.1%) | 1,114 (0.8%) | 357 (1.7%) | 3,164 (0.7%) | 758 (1.7%) | 5,796 (0.8%) | 1,531 (1.8%) | -0.09 |
| Past use of AGIs ; n (%) | 241 (0.2%) | 32 (0.2%) | 186 (0.1%) | 33 (0.2%) | 870 (0.2%) | 82 (0.2%) | 1,297 (0.2%) | 147 (0.2%) | 0.00 |
| Past use of Glitazones ; n (%) | 5,951 (4.3%) | 613 (3.2%) | 7,810 (5.4%) | 895 (4.3%) | 14,879 (3.3%) | 1,202 (2.7%) | 28,640 (3.9%) | 2,710 (3.2%) | 0.04 |
| Past use of 2nd Generation SUs; n (%) | 11,899 (8.6%) | 1,526 (7.8%) | 11,721 (8.2%) | 1,708 (8.1%) | 39,000 (8.6%) | 3,849 (8.6%) | 62,620 (8.5%) | 7,083 (8.3%) | 0.01 |
| Past use of Insulin ; n (%) | 3,859 (2.8%) | 1,402 (7.2%) | 3,613 (2.5%) | 1,446 (6.9%) | 14,951 (3.3%) | 3,549 (7.9%) | 22,423 (3.0%) | 6,397 (7.5%) | -0.20 |
| Past use of Meglitinides ; n (%) | 513 (0.4%) | 79 (0.4%) | 778 (0.5%) | 110 (0.5%) | 2,466 (0.5%) | 222 (0.5%) | 3,757 (0.5%) | 411 (0.5%) | 0.00 |
| Past use of metformin (final) ; n (%) | 14,973 (10.9%) | 2,324 (11.9%) | 14,940 (10.4%) | 2,720 (12.9%) | 49,628 (10.9%) | 5,339 (11.9%) | 79,541 (10.8%) | 10,383 (12.2%) | -0.04 |
| Other Medications | | | | | | | | | |
| Use of ACE inhibitors; n (%) | 64,855 (47.1%) | 8,724 (44.8%) | 66,162 (46.2%) | 9,336 (44.4%) | 205,264 (45.1%) | 19,889 (44.4%) | 336,281 (45.7%) | 37,949 (44.5%) | 0.02 |
| Use of ARBs; n (%) | 43,355 (31.5%) | 6,562 (33.7%) | 47,088 (32.9%) | 7,639 (36.3%) | 151,976 (33.4%) | 15,859 (35.4%) | 242,419 (33.0%) | 30,060 (35.2%) | -0.05 |
| Use of Loop Diuretics - United; n (%) | 22,407 (16.3%) | 3,599 (18.5%) | 22,391 (15.6%) | 3,594 (17.1%) | 98,566 (21.7%) | 9,891 (22.1%) | 143,364 (19.5%) | 17,084 (20.0%) | -0.01 |
| Use of other diuretics- United; n (%) | 4,749 (3.5%) | 912 (4.7%) | 5,277 (3.7%) | 970 (4.6%) | 18,328 (4.0%) | 2,185 (4.9%) | 28,354 (3.9%) | 4,067 (4.8%) | -0.04 |
| Use of nitrates-United; n (%) | 9,362 (6.8%) | 1,414 (7.3%) | 11,234 (7.8%) | 1,585 (7.5%) | 40,868 (9.0%) | 3,563 (8.0%) | 61,464 (8.4%) | 6,562 (7.7%) | 0.03 |
| Use of other hypertension drugs; n (%) | 12,044 (8.7%) | 1,520 (7.8%) | 11,547 (8.1%) | 1,498 (7.1%) | 44,046 (9.7%) | 3,845 (8.6%) | 67,637 (9.2%) | 6,863 (8.0%) | 0.04 |
| Use of digoxin- United; n (%) | 3,440 (2.5%) | 325 (1.7%) | 4,412 (3.1%) | 397 (1.9%) | 17,606 (3.9%) | 1,026 (2.3%) | 25,458 (3.5%) | 1,748 (2.0%) | 0.09 |
| Use of Anti-arrhythmics; n (%) | 2,573 (1.9%) | 343 (1.8%) | 3,016 (2.1%) | 359 (1.7%) | 11,844 (2.6%) | 978 (2.2%) | 17,433 (2.4%) | 1,680 (2.0%) | 0.03 |
| Use of COPD/asthma meds- United; n (%) | 21,727 (15.8%) | 3,388 (17.4%) | 22,229 (15.5%) | 3,787 (18.0%) | 83,884 (18.4%) | 8,641 (19.3%) | 127,840 (17.4%) | 15,816 (18.5%) | -0.03 |
| Use of statins; n (%) | 98,588 (71.6%) | 14,035 (72.1%) | 100,854 (70.4%) | 15,110 (71.8%) | 328,079 (72.2%) | 32,658 (72.9%) | 527,521 (71.7%) | 61,803 (72.5%) | -0.02 |
| Use of other lipid-lowering drugs; n (%) | 17,895 (13.0%) | 2,774 (14.3%) | 23,475 (16.4%) | 3,929 (18.7%) | 60,974 (13.4%) | 6,846 (15.3%) | 102,344 (13.9%) | 13,549 (15.9%) | -0.06 |
| Use of antiplatelet agents; n (%) | 20,986 (15.2%) | 3,009 (15.5%) | 27,448 (19.1%) | 4,060 (19.3%) | 79,242 (17.4%) | 7,048 (15.7%) | 127,676 (17.4%) | 14,117 (16.6%) | 0.02 |
| Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%) | 10,989 (8.0%) | 1,483 (7.6%) | 11,524 (8.0%) | 1,393 (6.6%) | 49,547 (10.9%) | 4,301 (9.6%) | 72,060 (9.8%) | 7,177 (8.4%) | 0.05 |
| Use of heparin and other low-molecular weight heparins; n (%) | 670 (0.5%) | 109 (0.6%) | 47 (0.0%) | 1 (0.0%) | 2,464 (0.5%) | 208 (0.5%) | 3,181 (0.4%) | 318 (0.4%) | 0.00 |
| Use of NSAIDs; n (%) | 21,041 (15.3%) | 3,463 (17.8%) | 21,453 (15.0%) | 3,650 (17.3%) | 78,824 (17.3%) | 8,045 (18.0%) | 121,318 (16.5%) | 15,158 (17.8%) | -0.03 |
| Use of oral corticosteroids; n (%) | 21,735 (15.8%) | 3,298 (16.9%) | 22,026 (15.4%) | 3,318 (15.8%) | 83,442 (18.4%) | 8,085 (18.1%) | 127,203 (17.3%) | 14,701 (17.2%) | 0.00 |
| Use of bisphosphonate (United); n (%) | 4,679 (3.4%) | 350 (1.8%) | 3,102 (2.2%) | 310 (1.5%) | 20,383 (4.5%) | 1,052 (2.3%) | 28,164 (3.8%) | 1,712 (2.0%) | 0.11 |
| Use of opioids- United; n (%) | 32,642 (23.7%) | 5,647 (29.0%) | 35,653 (24.9%) | 6,129 (29.1%) | 117,214 (25.8%) | 13,198 (29.5%) | 185,509 (25.2%) | 24,974 (29.3%) | -0.09 |
| Use of antidepressants; n (%) | 30,300 (22.0%) | 6,060 (31.1%) | 29,496 (20.6%) | 6,202 (29.5%) | 116,636 (25.7%) | 14,399 (32.2%) | 176,432 (24.0%) | 26,661 (31.3%) | -0.16 |
| Use of antipsychotics; n (%) | 3,211 (2.3%) | 453 (2.3%) | 2,529 (1.8%) | 370 (1.8%) | 17,910 (3.9%) | 1,052 (2.3%) | 23,650 (3.2%) | 1,875 (2.2%) | 0.06 |
| Use of anticonvulsants; n (%) | 20,811 (15.1%) | 4,095 (21.0%) | 16,587 (11.6%) | 3,194 (15.2%) | 78,878 (17.3%) | 8,935 (20.0%) | 116,276 (15.8%) | 16,224 (19.0%) | -0.08 |
| Use of lithium- United; n (%) | 152 (0.1%) | 22 (0.1%) | 153 (0.1%) | 27 (0.1%) | 574 (0.1%) | 55 (0.1%) | 879 (0.1%) | 104 (0.1%) | 0.00 |
| Use of Benzos- United; n (%) | 11,760 (8.5%) | 2,281 (11.7%) | 14,941 (10.4%) | 2,594 (12.3%) | 45,770 (10.1%) | 4,990 (11.1%) | 72,471 (9.9%) | 9,865 (11.6%) | -0.05 |
| Use of anxiolytics/hypnotics- United; n (%) | 7,916 (5.8%) | 1,425 (7.3%) | 9,470 (6.6%) | 1,735 (8.2%) | 31,510 (6.9%) | 3,415 (7.6%) | 48,896 (6.6%) | 6,575 (7.7%) | -0.04 |
| Use of dementia meds- United; n (%) | 4,155 (3.0%) | 205 (1.1%) | 3,015 (2.1%) | 147 (0.7%) | 27,566 (6.1%) | 918 (2.1%) | 34,736 (4.7%) | 1,270 (1.5%) | 0.19 |
| Use of antiparkinsonian meds- United; n (%) | 3,405 (2.5%) | 689 (3.5%) | 3,131 (2.2%) | 651 (3.1%) | 15,911 (3.5%) | 1,828 (4.1%) | 22,447 (3.1%) | 3,168 (3.7%) | -0.03 |
| Any use of pramlintide; n (%) | 5 (0.0%) | 17 (0.0%) | 17 (0.0%) | 30 (0.1%) | 18 (0.0%) | 19 (0.0%) | 040 (0.0%) | 054 (0.0%) | -0.04 |
| Any use of 1st generation sulfonylureas; n (%) | 26 (0.0%) | 0 (0.0%) | 35 (0.0%) | 1 (0.0%) | 80 (0.0%) | 4 (0.0%) | 141 (0.0%) | 005 (0.0%) | 0.00 |
| Entresto (sacubitril/valsartan); n (%) | 216 (0.2%) | 49 (0.3%) | 65 (0.0%) | 13 (0.1%) | 267 (0.1%) | 27 (0.1%) | 548 (0.1%) | 089 (0.1%) | 0.00 |
| Initiation as monotherapy ; n (%) | 15,454 (11.2%) | 0 (0.0%) | 15,217 (10.6%) | 0 (0.0%) | 42,437 (9.3%) | 0 (0.0%) | 73,108 (9.9%) | #VALUE! | #VALUE! |
| Labs | | | | | | | | | |
| Lab values- HbA1c (%); n (%) | 50,437 (36.6%) | 7,316 (37.6%) | 8,493 (5.9%) | 1,188 (5.6%) | N/A | N/A | 58,930 (21.0%) | 8,504 (21.0%) | 0.00 |
| Lab values- HbA1c (%) (within 3 months); n (%) | 39,878 (29.0%) | 5,615 (28.9%) | 6,736 (4.7%) | 933 (4.4%) | N/A | N/A | 46,614 (16.6%) | 6,548 (16.2%) | 0.01 |
| Lab values- HbA1c (%) (within 6 months); n (%) | 50,437 (36.6%) | 7,316 (37.6%) | 8,493 (5.9%) | 1,188 (5.6%) | N/A | N/A | 58,930 (21.0%) | 8,504 (21.0%) | 0.00 |
| Lab values- BNP; n (%) | 1,367 (1.0%) | 208 (1.1%) | 207 (0.1%) | 35 (0.2%) | N/A | N/A | 1,574 (0.6%) | 243 (0.6%) | 0.00 |
| Lab values- BNP (within 3 months); n (%) | 859 (0.6%) | 122 (0.6%) | 133 (0.1%) | 28 (0.1%) | N/A | N/A | 992 (0.4%) | 150 (0.4%) | 0.00 |
| Lab values- BNP (within 6 months); n (%) | 1,367 (1.0%) | 208 (1.1%) | 207 (0.1%) | 35 (0.2%) | N/A | N/A | 1,574 (0.6%) | 243 (0.6%) | 0.00 |
| Lab values- BUN (mg/dl); n (%) | 51,823 (37.6%) | 7,494 (38.5%) | 8,517 (5.9%) | 1,204 (5.7%) | N/A | N/A | 60,340 (21.5%) | 8,698 (21.5%) | 0.00 |
| Lab values- BUN (mg/dl) (within 3 months); n (%) | 40,495 (29.4%) | 5,663 (29.1%) | 6,596 (4.6%) | 918 (4.4%) | N/A | N/A | 47,091 (16.8%) | 6,581 (16.2%) | 0.02 |
| Lab values- BUN (mg/dl) (within 6 months); n (%) | 51,823 (37.6%) | 7,494 (38.5%) | 8,517 (5.9%) | 1,204 (5.7%) | N/A | N/A | 60,340 (21.5%) | 8,698 (21.5%) | 0.00 |
| Lab values- Creatinine (mg/dl); n (%) | 53,070 (38.6%) | 7,701 (39.6%) | 8,888 (6.2%) | 1,253 (6.0%) | N/A | N/A | 61,958 (22.1%) | 8,954 (22.1%) | 0.00 |
| Lab values- Creatinine (mg/dl) (within 3 months); n (%) | 41,526 (30.2%) | 5,821 (29.9%) | 6,892 (4.8%) | 950 (4.5%) | N/A | N/A | 48,418 (17.2%) | 6,771 (16.7%) | 0.01 |
| Lab values- Creatinine (mg/dl) (within 6 months); n (%) | 53,070 (38.6%) | 7,701 (39.6%) | 8,888 (6.2%) | 1,253 (6.0%) | N/A | N/A | 61,958 (22.1%) | 8,954 (22.1%) | 0.00 |
| Lab values- HDL level (mg/dl); n (%) | 43,367 (31.5%) | 6,185 (31.8%) | 7,438 (5.2%) | 1,046 (5.0%) | N/A | N/A | 50,805 (18.1%) | 7,231 (17.9%) | 0.01 |
| Lab values- HDL level (mg/dl) (within 3 months); n (%) | 31,824 (23.1%) | 4,395 (22.6%) | 5,475 (3.8%) | 765 (3.6%) | N/A | N/A | 37,299 (13.3%) | 5,160 (12.7%) | 0.02 |
| Lab values- HDL level (mg/dl) (within 6 months); n (%) | 43,367 (31.5%) | 6,185 (31.8%) | 7,438 (5.2%) | 1,046 (5.0%) | N/A | N/A | 50,805 (18.1%) | 7,231 (17.9%) | 0.01 |
| Lab values- LDL level (mg/dl); n (%) | 44,416 (32.3%) | 6,396 (32.9%) | 7,816 (5.5%) | 1,106 (5.3%) | N/A | N/A | 52,232 (18.6%) | 7,502 (18.5%) | 0.00 |
| Lab values- LDL level (mg/dl) (within 3 months); n (%) | 32,596 (23.7%) | 4,554 (23.4%) | 5,755 (4.0%) | 803 (3.8%) | N/A | N/A | 38,351 (13.6%) | 5,357 (13.2%) | 0.01 |
| Lab values- LDL level (mg/dl) (within 6 months); n (%) | 44,416 (32.3%) | 6,396 (32.9%) | 7,816 (5.5%) | 1,106 (5.3%) | N/A | N/A | 52,232 (18.6%) | 7,502 (18.5%) | 0.00 |
| Lab values- NT-proBNP; n (%) | 203 (0.1%) | 36 (0.2%) | 20 (0.0%) | 3 (0.0%) | N/A | N/A | 223 (0.1%) | 39 (0.1%) | 0.00 |
| Lab values- NT-proBNP (within 3 months); n (%) | 125 (0.1%) | 23 (0.1%) | 14 (0.0%) | 1 (0.0%) | N/A | N/A | 139 (0.0%) | 24 (0.1%) | - |
| Lab values- NT-proBNP (within 6 months); n (%) | 203 (0.1%) | 36 (0.2%) | 20 (0.0%) | 3 (0.0%) | N/A | N/A | 223 (0.1%) | 39 (0.1%) | - |
| Lab values- Total cholesterol (mg/dl); n (%) | 43,827 (31.8%) | 6,311 (32.4%) | 7,593 (5.3%) | 1,060 (5.0%) | N/A | N/A | 51,420 (18.3%) | 7,371 (18.2%) | 0.00 |
| Lab values- Total cholesterol (mg/dl) (within 3 months); n (%) | 32,199 (23.4%) | 4,492 (23.1%) | 5,597 (3.9%) | 775 (3.7%) | N/A | N/A | 37,796 (13.5%) | 5,267 (13.0%) | 0.01 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|---|-------------------------|-------------------------|-------|-------------------------|-------------------------|-------|-------------------|-------------------|---------|-------------------|------------------|---------|
| Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%) | 43,827 (31.8%) | 6,311 (32.4%) | | 7,593 (5.3%) | 1,060 (5.0%) | | N/A | N/A | | 51,420 (18.3%) | 7,371 (18.2%) | 0.00 |
| Lab values- Triglyceride level (mg/dl); n (%) | 43,538 (31.6%) | 6,253 (32.1%) | | 7,502 (5.2%) | 1,041 (4.9%) | | N/A | N/A | | 51,040 (18.2%) | 7,294 (18.0%) | 0.01 |
| Lab values- Triglyceride level (mg/dl) (within 3 months); n (%) | 31,997 (23.2%) | 4,455 (22.9%) | | 5,533 (3.9%) | 761 (3.6%) | | N/A | N/A | | 37,530 (13.4%) | 5,216 (12.9%) | 0.01 |
| Lab values- Triglyceride level (mg/dl) (within 6 months); n (%) | 43,538 (31.6%) | 6,253 (32.1%) | | 7,502 (5.2%) | 1,041 (4.9%) | | N/A | N/A | | 51,040 (18.2%) | 7,294 (18.0%) | 0.01 |
| Lab result number- HbA1c (%) mean (only 2 to 20 included) | 50,233 | 7,279 | | 8,105 | 1,124 | | N/A | N/A | | 58,338 | 8,403 | |
| ...mean (sd) | 7.95 (1.60) | 8.04 (1.73) | -0.05 | 7.97 (1.62) | 8.03 (1.73) | -0.04 | N/A | N/A | #VALUE! | 7.95 (1.60) | 8.04 (1.73) | -0.05 |
| ...median [IQR] | 7.60 [6.90, 8.65] | 7.70 [6.80, 8.95] | -0.06 | 7.60 [6.90, 8.70] | 7.75 [6.80, 8.95] | -0.09 | N/A | N/A | #VALUE! | 7.60 (1.60) | 7.71 (1.73) | -0.07 |
| ...Missing; n (%) | 87,416 (63.5%) | 12,181 (62.6%) | 0.02 | 135,232 (94.3%) | 19,917 (94.7%) | -0.02 | N/A | N/A | #VALUE! | 222,648 (79.2%) | 32,098 (79.3%) | 0.00 |
| Lab result number- BNP mean | 1,367 | 208 | | 207 | 35 | | N/A | N/A | | 1,574 | 243 | |
| ...mean (sd) | 202.08 (359.17) | 111.51 (209.59) | 0.31 | 1,686.84 (19,478.97) | 103.76 (169.94) | 0.11 | N/A | N/A | #VALUE! | 397.34 (7061.56) | 110.39 (204.89) | 0.06 |
| ...median [IQR] | 88.65 [33.40, 217.10] | 43.85 [20.85, 111.38] | 0.15 | 93.00 [34.00, 253.00] | 45.70 [17.00, 124.00] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 136,282 (99.0%) | 19,252 (98.9%) | 0.01 | 143,130 (99.9%) | 21,006 (99.8%) | 0.03 | N/A | N/A | #VALUE! | 279,412 (99.4%) | 40,258 (99.4%) | 0.00 |
| Lab result number- BUN (mg/dl) mean | 51,823 | 7,494 | | 8,517 | 1,204 | | N/A | N/A | | 60,340 | 8,698 | |
| ...mean (sd) | 19.96 (8.65) | 19.56 (8.25) | 0.05 | 296.19 (6,635.25) | 675.16 (11,808.66) | -0.04 | N/A | N/A | #VALUE! | 58.95 (2492.37) | 110.31 (4392.37) | -0.01 |
| ...median [IQR] | 18.00 [14.00, 23.00] | 18.00 [14.00, 23.00] | 0.00 | 17.50 [14.00, 22.00] | 18.00 [14.31, 22.00] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 85,826 (62.4%) | 11,966 (61.5%) | 0.02 | 134,820 (94.1%) | 19,837 (94.3%) | -0.01 | N/A | N/A | #VALUE! | 220,646 (78.5%) | 31,803 (78.5%) | 0.00 |
| Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) | 52,715 | 7,656 | | 8,281 | 1,142 | | N/A | N/A | | 60,996 | 8,798 | |
| ...mean (sd) | 1.08 (0.42) | 1.04 (0.37) | 0.10 | 1.06 (0.41) | 1.01 (0.32) | 0.14 | N/A | N/A | #VALUE! | 1.08 (0.42) | 1.04 (0.36) | 0.10 |
| ...median [IQR] | 0.99 [0.82, 1.25] | 0.97 [0.80, 1.20] | 0.05 | 0.99 [0.82, 1.18] | 0.97 [0.80, 1.14] | 0.05 | N/A | N/A | #VALUE! | 0.99 (0.42) | 0.97 (0.36) | 0.05 |
| ...Missing; n (%) | 84,934 (61.7%) | 11,804 (60.7%) | 0.02 | 135,056 (94.2%) | 19,899 (94.6%) | -0.02 | N/A | N/A | #VALUE! | 219,990 (78.3%) | 31,703 (78.3%) | 0.00 |
| Lab result number- HDL level (mg/dl) mean (only <=5000 included) | 43,367 | 6,185 | | 7,424 | 1,042 | | N/A | N/A | | 50,791 | 7,227 | |
| ...mean (sd) | 47.10 (13.82) | 45.86 (13.11) | 0.09 | 45.00 [14.90] | 44.44 [13.95] | 0.04 | N/A | N/A | #VALUE! | 46.79 [13.98] | 45.66 [13.24] | 0.08 |
| ...median [IQR] | 45.00 [38.00, 54.00] | 44.00 [37.00, 53.00] | 0.07 | 43.50 [36.00, 52.00] | 43.00 [36.00, 52.00] | 0.03 | N/A | N/A | #VALUE! | 44.78 [13.98] | 43.86 [13.24] | 0.07 |
| ...Missing; n (%) | 94,282 (68.5%) | 13,275 (68.2%) | 0.01 | 135,913 (94.8%) | 19,999 (95.0%) | -0.01 | N/A | N/A | #VALUE! | 230,195 (81.9%) | 33,274 (82.2%) | -0.01 |
| Lab result number- LDL level (mg/dl) mean (only <=5000 included) | 43,555 | 6,264 | | 7,261 | 970 | | N/A | N/A | | 50,816 | 7,234 | |
| ...mean (sd) | 84.65 (36.88) | 82.02 (37.07) | 0.07 | 85.59 (39.45) | 83.80 (40.29) | 0.04 | N/A | N/A | #VALUE! | 84.78 (37.26) | 82.26 (37.52) | 0.07 |
| ...median [IQR] | 81.00 [62.00, 105.00] | 79.00 [60.00, 102.00] | 0.05 | 83.00 [63.00, 108.00] | 83.83 [62.00, 106.00] | -0.02 | N/A | N/A | #VALUE! | 81.29 (37.26) | 79.65 (37.52) | 0.04 |
| ...Missing; n (%) | 94,094 (68.4%) | 13,196 (67.8%) | 0.01 | 136,076 (94.9%) | 20,071 (95.4%) | -0.02 | N/A | N/A | #VALUE! | 230,170 (81.9%) | 33,267 (82.1%) | -0.01 |
| Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) | 43,788 | 6,307 | | 7,574 | 1,055 | | N/A | N/A | | 51,362 | 7,362 | |
| ...mean (sd) | 168.90 (43.18) | 167.72 (42.61) | 0.03 | 169.13 (49.20) | 170.60 (48.43) | -0.03 | N/A | N/A | #VALUE! | 168.93 (44.12) | 168.13 (43.49) | 0.02 |
| ...median [IQR] | 163.00 [140.00, 192.00] | 162.00 [139.00, 191.00] | 0.02 | 165.50 [141.00, 195.00] | 166.00 [143.00, 196.00] | -0.01 | N/A | N/A | #VALUE! | 163.37 (44.12) | 162.57 (43.49) | 0.02 |
| ...Missing; n (%) | 93,861 (68.2%) | 13,153 (67.6%) | 0.01 | 135,763 (94.7%) | 19,986 (95.0%) | -0.01 | N/A | N/A | #VALUE! | 229,624 (81.7%) | 33,139 (81.8%) | 0.00 |
| Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) | 43,537 | 6,253 | | 7,487 | 1,037 | | N/A | N/A | | 51,024 | 7,290 | |
| ...mean (sd) | 174.08 (126.30) | 184.98 (134.65) | -0.08 | 177.97 (145.09) | 188.26 (149.15) | -0.07 | N/A | N/A | #VALUE! | 174.65 (129.23) | 185.45 (136.81) | -0.08 |
| ...median [IQR] | 147.00 [106.00, 207.00] | 155.00 [112.00, 218.25] | -0.06 | 147.00 [104.00, 211.00] | 155.00 [108.75, 222.50] | -0.05 | N/A | N/A | #VALUE! | 147.00 (129.23) | 155.00 (136.81) | -0.06 |
| ...Missing; n (%) | 94,112 (68.4%) | 13,207 (67.9%) | 0.01 | 135,850 (94.8%) | 20,004 (95.1%) | -0.01 | N/A | N/A | #VALUE! | 229,962 (81.8%) | 33,211 (82.0%) | -0.01 |
| Lab result number- Hemoglobin mean (only >0 included) | 37,026 | 5,160 | | 5,743 | 800 | | N/A | N/A | | 42,769 | 5,960 | |
| ...mean (sd) | 13.23 (1.68) | 13.43 (1.61) | -0.12 | 6,480.13 (237,920.16) | 13.29 (2.45) | 0.04 | N/A | N/A | #VALUE! | 881.60 (87179.33) | 13.41 (1.75) | 0.01 |
| ...median [IQR] | 13.30 [12.10, 14.40] | 13.40 [12.40, 14.50] | -0.06 | 13.43 [12.30, 14.60] | 13.45 [12.40, 14.70] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | 13.41 (1.75) | #VALUE! |
| ...Missing; n (%) | 100,623 (73.1%) | 14,300 (73.5%) | -0.01 | 137,594 (96.0%) | 20,241 (96.2%) | -0.01 | N/A | N/A | #VALUE! | 238,217 (84.8%) | 34,541 (85.3%) | -0.01 |
| Lab result number- Serum sodium mean (only >90 and < 190 included) | 51,647 | 7,503 | | 8,075 | 1,118 | | N/A | N/A | | 59,722 | 8,621 | |
| ...mean (sd) | 139.46 (2.75) | 139.63 (2.63) | -0.06 | 139.06 (2.61) | 139.07 (2.53) | 0.00 | N/A | N/A | #VALUE! | 139.41 (2.73) | 139.56 (2.62) | -0.06 |
| ...median [IQR] | 139.67 [138.00, 141.00] | 140.00 [138.00, 141.33] | -0.12 | 139.00 [137.50, 141.00] | 139.00 [137.50, 141.00] | 0.00 | N/A | N/A | #VALUE! | 139.58 (2.73) | 139.87 (2.62) | -0.11 |
| ...Missing; n (%) | 86,002 (62.5%) | 11,957 (61.4%) | 0.02 | 135,262 (94.4%) | 19,923 (94.7%) | -0.01 | N/A | N/A | #VALUE! | 221,264 (78.7%) | 31,880 (78.7%) | 0.00 |
| Lab result number- Albumin mean (only >0 and <=10 included) | 48,037 | 6,977 | | 7,159 | 1,043 | | N/A | N/A | | 55,196 | 8,020 | |
| ...mean (sd) | 4.23 (0.32) | 4.22 (0.31) | 0.03 | 4.15 (0.61) | 4.10 (0.69) | 0.08 | N/A | N/A | #VALUE! | 4.22 (0.37) | 4.20 (0.38) | 0.05 |
| ...median [IQR] | 4.25 [4.03, 4.40] | 4.20 [4.00, 4.40] | 0.16 | 4.20 [4.00, 4.43] | 4.20 [4.00, 4.40] | 0.00 | N/A | N/A | #VALUE! | 4.24 (0.37) | 4.20 (0.38) | 0.11 |
| ...Missing; n (%) | 89,612 (65.1%) | 12,483 (64.1%) | 0.02 | 136,178 (95.0%) | 19,998 (95.0%) | 0.00 | N/A | N/A | #VALUE! | 225,790 (80.4%) | 32,481 (80.2%) | 0.01 |
| Lab result number- Glucose (fasting or random) mean (only 10-1000 included) | 51,675 | 7,479 | | 7,923 | 1,101 | | N/A | N/A | | 59,598 | 8,580 | |
| ...mean (sd) | 165.49 (64.13) | 166.85 (68.45) | -0.02 | 166.86 (64.34) | 167.95 (68.62) | -0.02 | N/A | N/A | #VALUE! | 165.67 (64.16) | 166.99 (68.48) | -0.02 |
| ...median [IQR] | 151.00 [123.00, 191.00] | 151.33 [119.00, 196.50] | 0.00 | 152.00 [123.50, 193.00] | 152.00 [119.00, 197.50] | 0.00 | N/A | N/A | #VALUE! | 151.13 [64.16] | 151.42 (68.48) | 0.00 |
| ...Missing; n (%) | 85,974 (62.5%) | 11,981 (61.6%) | 0.02 | 135,414 (94.5%) | 19,940 (94.8%) | -0.01 | N/A | N/A | #VALUE! | 221,388 (78.8%) | 31,921 (78.8%) | 0.00 |
| Lab result number- Potassium mean (only 1-7 included) | 52,631 | 7,654 | | 8,344 | 1,170 | | N/A | N/A | | 60,975 | 8,824 | |
| ...mean (sd) | 4.46 (0.45) | 4.46 (0.43) | 0.00 | 4.38 (0.45) | 4.36 (0.46) | 0.04 | N/A | N/A | #VALUE! | 4.45 (0.45) | 4.45 (0.43) | 0.00 |
| ...median [IQR] | 4.45 [4.20, 4.70] | 4.45 [4.20, 4.70] | 0.00 | 4.40 [4.10, 4.65] | 4.35 [4.00, 4.60] | 0.11 | N/A | N/A | #VALUE! | 4.44 (0.45) | 4.44 (0.43) | 0.00 |
| ...Missing; n (%) | 85,018 (61.8%) | 11,806 (60.7%) | 0.02 | 134,993 (94.2%) | 19,871 (94.4%) | -0.01 | N/A | N/A | #VALUE! | 220,011 (78.3%) | 31,677 (78.2%) | 0.00 |
| Comorbidity Scores | | | | | | | | | | | | |
| CCI (180 days)- ICD9 and ICD10 | | | | | | | | | | | | |
| ...mean (sd) | 2.97 (2.15) | 2.83 (1.89) | 0.07 | 2.25 (1.79) | 2.11 (1.55) | 0.08 | 3.28 (2.42) | 2.88 (1.99) | 0.18 | 3.02 (2.26) | 2.68 (1.87) | 0.16 |
| ...median [IQR] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 0.00 | 2.00 [1.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 3.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 0.45 | 2.62 (2.26) | 2.00 (1.87) | 0.30 |
| Frailty Score: Qualitative Version 365 days as Categories, v1 | | | | | | | | | | | | |
| ...0; n (%) | 58,642 (42.6%) | 9,778 (50.2%) | -0.15 | 42,071 (29.4%) | 6,451 (30.7%) | -0.03 | 124,218 (27.3%) | 15,058 (33.6%) | -0.14 | 224,931 (30.6%) | 31,287 (36.7%) | -0.13 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|--|---------------------|---------------------|-------|--------------------|---------------------|-------|---------------------|---------------------|-------|-----------------|----------------|-------|
| ...to 2; n (%) | 48,415 (35.2%) | 6,258 (32.2%) | 0.06 | 62,110 (43.3%) | 9,391 (44.6%) | -0.03 | 154,631 (34.0%) | 15,118 (33.8%) | 0.00 | 265,156 (36.0%) | 30,767 (36.1%) | 0.00 |
| ...3 or more; n (%) | 30,592 (22.2%) | 3,424 (17.6%) | 0.12 | 39,156 (27.3%) | 5,199 (24.7%) | 0.06 | 175,851 (38.7%) | 14,602 (32.6%) | 0.13 | 245,599 (33.4%) | 23,225 (27.2%) | 0.14 |
| Frailty Score: Empirical Version 365 days as Categories, | | | | | | | | | | | | |
| ...< 0.12908; n (%) | 26,302 (19.1%) | 3,419 (17.6%) | 0.04 | 25,022 (17.5%) | 3,502 (16.6%) | 0.02 | 40,499 (8.9%) | 4,069 (9.1%) | -0.01 | 91,823 (12.5%) | 10,990 (12.9%) | -0.01 |
| ...0.12908 - 0.1631167; n (%) | 43,259 (31.4%) | 6,091 (31.3%) | 0.00 | 45,778 (31.9%) | 6,848 (32.5%) | -0.01 | 100,081 (22.0%) | 10,744 (24.0%) | -0.05 | 189,118 (25.7%) | 23,683 (27.8%) | -0.05 |
| ...>= 0.1631167; n (%) | 68,088 (49.5%) | 9,950 (50.8%) | -0.03 | 72,537 (50.6%) | 10,691 (50.8%) | 0.00 | 314,120 (69.1%) | 29,965 (66.9%) | 0.05 | 454,745 (61.8%) | 50,606 (59.3%) | 0.05 |
| Non-Frailty; n (%) | 82,389 (59.9%) | 12,060 (62.0%) | -0.04 | 77,838 (54.3%) | 11,838 (56.3%) | -0.04 | 18,822 (4.1%) | 1,899 (4.2%) | -0.01 | 179,049 (24.3%) | 25,797 (30.3%) | -0.13 |
| Frailty Score (mean): Qualitative Version 365 days, v1 | | | | | | | | | | | | |
| ...mean (sd) | 1.52 (2.04) | 1.19 (1.72) | 0.17 | 1.82 (1.97) | 1.65 (1.71) | 0.09 | 2.43 (2.56) | 1.96 (2.17) | 0.20 | 2.14 (2.36) | 1.71 (1.97) | 0.20 |
| ...median [IQR] | 1.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.53 | 1.00 [0.00, 3.00] | 1.00 [0.00, 2.00] | 0.00 | 2.00 [0.00, 4.00] | 1.00 [0.00, 3.00] | 0.42 | 1.62 (2.36) | 0.77 (1.97) | 0.39 |
| Frailty Score (mean): Empirical Version 365 days, | | | | | | | | | | | | |
| ...mean (sd) | 0.18 (0.06) | 0.18 (0.05) | 0.00 | 0.17 (0.05) | 0.17 (0.05) | 0.00 | 0.21 (0.07) | 0.20 (0.06) | 0.15 | 0.20 (0.06) | 0.19 (0.06) | 0.17 |
| ...median [IQR] | 0.16 [0.14, 0.20] | 0.16 [0.14, 0.20] | 0.00 | 0.16 [0.13, 0.19] | 0.16 [0.13, 0.19] | 0.00 | 0.19 [0.15, 0.24] | 0.18 [0.15, 0.23] | 0.15 | 0.18 (0.06) | 0.17 (0.06) | 0.17 |
| Healthcare Utilization | | | | | | | | | | | | |
| Any hospitalization; n (%) | 15,411 (11.2%) | 1,572 (8.1%) | | 17,629 (12.3%) | 1,789 (8.5%) | | 69,335 (15.2%) | 3,966 (8.9%) | | 102,375 (13.9%) | 7,327 (8.6%) | 0.17 |
| Any hospitalization within prior 30 days; n (%) | 5,707 (4.1%) | 323 (1.7%) | | 5,387 (3.8%) | 318 (1.5%) | | 25,040 (5.5%) | 770 (1.7%) | | 36,134 (4.9%) | 1,411 (1.7%) | 0.18 |
| Any hospitalization during prior 31-180 days; n (%) | 10,885 (7.9%) | 1,314 (6.8%) | | 13,146 (9.2%) | 1,527 (7.3%) | | 51,026 (11.2%) | 3,341 (7.5%) | | 75,057 (10.2%) | 6,182 (7.2%) | 0.11 |
| Endocrinologist Visit; n (%) | 12,664 (9.2%) | 4,174 (21.4%) | | 14,144 (9.9%) | 4,761 (22.6%) | | 50,811 (11.2%) | 11,071 (24.7%) | | 77,619 (10.6%) | 20,006 (23.5%) | -0.35 |
| Endocrinologist Visit (30 days prior); n (%) | 8,050 (5.8%) | 2,703 (13.9%) | | 9,334 (6.5%) | 3,309 (15.7%) | | 32,372 (7.1%) | 7,011 (15.7%) | | 49,756 (6.8%) | 13,023 (15.3%) | -0.27 |
| Endocrinologist Visit (31 to 180 days prior); n (%) | 8,644 (6.3%) | 2,970 (15.3%) | | 9,648 (6.7%) | 3,342 (15.9%) | | 35,496 (7.8%) | 8,312 (18.6%) | | 53,788 (7.3%) | 14,624 (17.1%) | -0.30 |
| Internal medicine/family medicine visits; n (%) | 121,361 (88.2%) | 16,269 (83.6%) | | 124,756 (87.0%) | 18,034 (85.7%) | | 387,047 (85.1%) | 37,552 (83.9%) | | 633,164 (86.1%) | 71,855 (84.3%) | 0.05 |
| Internal medicine/family medicine visits (30 days prior) ; n (%) | 94,520 (68.7%) | 11,561 (59.4%) | | 94,848 (66.2%) | 12,851 (61.1%) | | 290,265 (63.8%) | 25,156 (56.2%) | | 479,633 (65.2%) | 49,568 (58.1%) | 0.15 |
| Internal medicine/family medicine visits (31 to 180 days prior); n (%) | 110,003 (79.9%) | 14,957 (76.9%) | | 111,872 (78.0%) | 16,418 (78.0%) | | 347,879 (76.5%) | 34,444 (76.9%) | | 569,754 (77.4%) | 65,819 (77.2%) | 0.00 |
| Cardiologist visit; n (%) | 45,210 (32.8%) | 6,781 (34.8%) | | 45,236 (31.6%) | 7,080 (33.6%) | | 177,196 (39.0%) | 16,264 (36.3%) | | 267,642 (36.4%) | 30,125 (35.3%) | 0.02 |
| Number of Cardiologist visits (30 days prior); n (%) | 17,032 (12.4%) | 2,281 (11.7%) | | 16,404 (11.4%) | 2,355 (11.2%) | | 67,756 (14.9%) | 5,177 (11.6%) | | 101,192 (13.8%) | 9,813 (11.5%) | 0.07 |
| Number of Cardiologist visits (31 to 180 days prior); n (%) | 38,027 (27.6%) | 5,824 (29.9%) | | 38,469 (26.8%) | 6,074 (28.9%) | | 152,067 (33.4%) | 14,293 (31.9%) | | 228,563 (31.1%) | 26,191 (30.7%) | 0.01 |
| Electrocardiogram ; n (%) | 49,482 (35.9%) | 6,621 (34.0%) | | 54,504 (38.0%) | 7,572 (36.0%) | | 181,062 (39.8%) | 15,773 (35.2%) | | 285,048 (38.7%) | 29,966 (35.1%) | 0.07 |
| Use of glucose test strips; n (%) | 6,117 (4.4%) | 808 (4.2%) | | 5,867 (4.1%) | 1,004 (4.8%) | | 17,314 (3.8%) | 1,728 (3.9%) | | 29,298 (4.0%) | 3,540 (4.2%) | -0.01 |
| Dialysis; n (%) | 82 (0.1%) | 11 (0.1%) | | 136 (0.1%) | 9 (0.0%) | | 560 (0.1%) | 18 (0.0%) | | 778 (0.1%) | 038 (0.0%) | 0.04 |
| Naive new user v8 ; n (%) | 23,724 (17.2%) | 2,950 (15.2%) | | 23,744 (16.6%) | 2,590 (12.3%) | | 66,532 (14.6%) | 4,828 (10.8%) | | 114,000 (15.5%) | 10,368 (12.2%) | 0.10 |
| N antidiabetic drugs at index date | | | | | | | | | | | | |
| ...mean (sd) | 2.12 (0.81) | 2.07 (0.88) | 0.06 | 2.14 (0.81) | 2.10 (0.90) | 0.05 | 2.10 (0.79) | 2.11 (0.85) | -0.01 | 2.11 (0.80) | 2.10 (0.87) | 0.01 |
| ...median [IQR] | 2.00 [2.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 [2.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 [2.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 (0.80) | 2.00 (0.87) | 0.00 |
| Number of different/distinct medication prescriptions | | | | | | | | | | | | |
| ...mean (sd) | 10.45 (4.75) | 11.70 (5.14) | -0.25 | 10.12 (4.59) | 11.57 (4.91) | -0.31 | 10.69 (4.75) | 11.32 (4.71) | -0.13 | 10.53 (4.72) | 11.47 (4.86) | -0.20 |
| ...median [IQR] | 10.00 [7.00, 13.00] | 11.00 [8.00, 15.00] | -0.20 | 9.00 [7.00, 13.00] | 11.00 [8.00, 14.00] | -0.42 | 10.00 [7.00, 13.00] | 11.00 [8.00, 14.00] | -0.21 | 9.81 (4.72) | 11.00 (4.86) | -0.25 |
| Number of Hospitalizations | | | | | | | | | | | | |
| ...mean (sd) | 0.14 (0.46) | 0.10 (0.36) | 0.10 | 0.15 (0.43) | 0.10 (0.35) | 0.13 | 0.22 (0.61) | 0.11 (0.40) | 0.21 | 0.19 (0.55) | 0.11 (0.38) | 0.17 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (0.55) | 0.00 (0.38) | 0.00 |
| Number of hospital days | | | | | | | | | | | | |
| ...mean (sd) | 0.89 (4.08) | 0.49 (2.57) | 0.12 | 0.88 (4.03) | 0.47 (2.29) | 0.13 | 1.51 (5.72) | 0.63 (2.98) | 0.19 | 1.27 (5.15) | 0.56 (2.73) | 0.17 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (5.15) | 0.00 (2.73) | 0.00 |
| Number of Emergency Department (ED) visits | | | | | | | | | | | | |
| ...mean (sd) | 0.47 (1.31) | 0.41 (1.20) | 0.05 | 0.23 (1.55) | 0.16 (1.24) | 0.05 | 0.64 (1.56) | 0.45 (1.22) | 0.14 | 0.53 (1.51) | 0.37 (1.22) | 0.12 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (1.51) | 0.00 (1.22) | 0.00 |
| Number of Office visits | | | | | | | | | | | | |
| ...mean (sd) | 5.26 (3.96) | 5.84 (4.12) | -0.14 | 5.47 (4.09) | 6.07 (4.31) | -0.14 | 5.82 (4.49) | 6.47 (4.62) | -0.14 | 5.65 (4.32) | 6.23 (4.43) | -0.13 |
| ...median [IQR] | 4.00 [3.00, 7.00] | 5.00 [3.00, 8.00] | -0.25 | 4.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | -0.24 | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 0.00 | 4.62 (4.32) | 5.00 (4.40) | -0.09 |
| Number of Endocrinologist visits | | | | | | | | | | | | |
| ...mean (sd) | 0.43 (2.15) | 1.12 (3.61) | -0.23 | 0.46 (2.24) | 1.18 (3.69) | -0.24 | 0.64 (3.15) | 1.63 (5.11) | -0.23 | 0.57 (2.82) | 1.40 (4.48) | -0.22 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (2.82) | 0.00 (4.48) | 0.00 |
| Number of internal medicine/family medicine visits | | | | | | | | | | | | |
| ...mean (sd) | 11.36 (14.86) | 10.41 (14.29) | 0.07 | 8.00 (10.30) | 7.77 (9.67) | 0.02 | 9.44 (12.00) | 8.75 (11.42) | 0.06 | 9.52 (12.29) | 8.89 (11.75) | 0.05 |
| ...median [IQR] | 7.00 [3.00, 15.00] | 6.00 [2.00, 13.00] | 0.07 | 5.00 [2.00, 10.00] | 5.00 [2.00, 10.00] | 0.00 | 6.00 [2.00, 13.00] | 5.00 [2.00, 12.00] | 0.09 | 5.99 (12.29) | 5.23 (11.75) | 0.06 |
| Number of Cardiologist visits | | | | | | | | | | | | |
| ...mean (sd) | 1.74 (4.43) | 1.71 (4.03) | 0.01 | 1.49 (3.77) | 1.54 (3.73) | -0.01 | 2.31 (5.55) | 1.97 (4.90) | 0.06 | 2.04 (5.05) | 1.80 (4.44) | 0.05 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 (5.05) | 0.00 (4.44) | 0.00 |
| Number electrocardiograms received | | | | | | | | | | | | |
| ...mean (sd) | 0.76 (1.64) | 0.67 (1.47) | 0.06 | 0.71 (1.34) | 0.64 (1.21) | 0.05 | 0.89 (1.66) | 0.70 (1.34) | 0.13 | 0.83 (1.60) | 0.68 (1.34) | 0.10 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 (1.60) | 0.00 (1.34) | 0.00 |
| Number of HbA1c tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 1.35 (0.93) | 1.40 (0.92) | -0.05 | 0.98 (0.94) | 1.15 (0.95) | -0.18 | 1.44 (0.91) | 1.53 (0.88) | -0.10 | 1.33 (0.92) | 1.41 (0.91) | -0.09 |
| ...median [IQR] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 0.00 | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 (0.92) | 1.00 (0.91) | 0.00 |
| Number of glucose tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 0.60 (2.85) | 0.57 (1.41) | 0.01 | 0.43 (1.50) | 0.50 (1.20) | -0.05 | 0.49 (1.20) | 0.51 (1.13) | -0.02 | 0.50 (1.69) | 0.52 (1.22) | -0.01 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 (1.69) | 0.00 (1.22) | 0.00 |
| Number of lipid tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 1.08 (1.01) | 1.08 (1.01) | 0.00 | 0.86 (1.31) | 1.00 (1.31) | -0.11 | 1.07 (0.86) | 1.11 (0.88) | -0.05 | 1.03 (0.99) | 1.08 (1.03) | -0.05 |
| ...median [IQR] | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 0.00 | 1.00 [0.00, 1.00] | 1.00 [0.00, 1.00] | 0.00 | 1.00 [0.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 (0.99) | 1.00 (1.03) | 0.00 |
| Number of creatinine tests ordered | | | | | | | | | | | | |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|--|-------------------|--------------------|--------------|-------------------|-------------------|-------------|-------------------|--------------------|-------------|-----------------|----------------|-------|
| ...mean (sd) | 0.06 (0.35) | 0.06 (0.30) | 0.00 | 0.06 (0.35) | 0.06 (0.34) | 0.00 | 0.09 (0.39) | 0.10 (0.41) | -0.02 | 0.08 (0.38) | 0.08 (0.37) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (0.38) | 0.00 (0.37) | 0.00 |
| Number of BUN tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 0.04 (0.28) | 0.03 (0.23) | 0.04 | 0.04 (0.29) | 0.04 (0.27) | 0.00 | 0.06 (0.32) | 0.06 (0.32) | 0.00 | 0.05 (0.31) | 0.05 (0.29) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (0.31) | 0.00 (0.29) | 0.00 |
| Number of tests for microalbuminuria | | | | | | | | | | | | |
| ...mean (sd) | 0.82 (1.23) | 0.87 (1.25) | -0.04 | 0.52 (0.99) | 0.64 (1.07) | -0.12 | 0.49 (0.73) | 0.56 (0.77) | -0.09 | 0.56 (0.90) | 0.65 (0.97) | -0.10 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 (0.90) | 0.00 (0.97) | 0.00 |
| Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level | | | | | | | | | | | | |
| ...mean (sd) | 5.98 (8.59) | 7.00 (8.44) | -0.12 | 2.59 (5.59) | 2.39 (4.66) | 0.04 | 6.46 (9.71) | 6.21 (8.58) | 0.03 | 5.62 (8.84) | 5.45 (7.76) | 0.02 |
| ...median [IQR] | 4.00 [0.00, 9.00] | 5.00 [0.00, 10.00] | -0.12 | 0.00 [0.00, 4.00] | 0.00 [0.00, 4.00] | 0.00 | 3.00 [0.00, 9.00] | 3.00 [0.00, 10.00] | 0.00 | 2.60 (8.84) | 2.72 (7.76) | -0.01 |
| Use of thiazide; n (%) | 19,082 (13.9%) | 2,749 (14.1%) | -0.005763928 | 18,570 (13.0%) | 2,811 (13.4%) | -0.01181737 | 66,785 (14.7%) | 6,981 (15.6%) | -0.02510409 | 104,437 (14.2%) | 12,541 (14.7%) | -0.01 |
| Use of beta blockers; n (%) | 62,221 (45.2%) | 8,804 (45.2%) | 0.00 | 67,518 (47.1%) | 9,653 (45.9%) | 0.02 | 233,117 (51.3%) | 21,826 (48.7%) | 0.05 | 362,856 (49.3%) | 40,283 (47.2%) | 0.04 |
| Use of calcium channel blockers; n (%) | 46,524 (33.8%) | 5,822 (29.9%) | 0.08 | 46,777 (32.6%) | 6,355 (30.2%) | 0.05 | 167,449 (36.8%) | 14,468 (32.3%) | 0.09 | 260,750 (35.4%) | 26,645 (31.2%) | 0.09 |

Table 1: Liraglutide vs DPP4i

| PS-matched | | | | | | | | | | | |
|---|----------------------|-----------------------|-----------|----------------------|-----------------------|-----------|----------------------|-----------------------|-----------|------------------|-----------------------|
| | Optum | | | MarketScan | | | Medicare | | | POOLED | |
| Variable | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | Exposure- Liraglutide | St. Diff. | Reference- DPP4i | Exposure- Liraglutide |
| Number of patients | 19187 | 19187 | | 20777 | 20777 | | 44381 | 44381 | | 84,345 | 84,345 |
| Age | | | | | | | | | | | |
| ...mean (sd) | 65.88 (7.35) | 66.08 (6.82) | -0.03 | 62.98 (6.89) | 63.12 (6.32) | -0.02 | 70.54 (5.22) | 70.62 (5.01) | -0.02 | 67.62 (6.19) | 67.74 (5.80) |
| ...median [IQR] | 66.00 [61.00, 70.00] | 66.00 [61.00, 70.00] | 0.00 | 62.00 [60.00, 66.00] | 62.00 [60.00, 66.00] | 0.00 | 69.00 [67.00, 73.00] | 69.00 [67.00, 73.00] | 0.00 | 66.59 (6.19) | 66.59 (5.80) |
| Age categories | | | | | | | | | | | |
| ...18 - 54; n (%) | 1,284 (6.7%) | 1,036 (5.4%) | 0.05 | 2,089 (10.1%) | 1,724 (8.3%) | 0.06 | 0 (0.0%) | 0 (0.0%) | #DIV/0! | 3,373 (4.0%) | 2,760 (3.3%) |
| ...55 - 64; n (%) | 6,997 (36.5%) | 6,760 (35.2%) | 0.03 | 12,548 (60.4%) | 12,685 (61.1%) | -0.01 | 1,434 (3.2%) | 1,078 (2.4%) | 0.05 | 20,979 (24.9%) | 20,523 (24.3%) |
| ...65 - 74; n (%) | 8,588 (44.8%) | 9,298 (48.5%) | -0.07 | 4,672 (22.5%) | 5,162 (24.8%) | -0.05 | 34,293 (77.3%) | 34,597 (78.0%) | -0.02 | 47,553 (56.4%) | 49,057 (58.2%) |
| ...≥ 75; n (%) | 2,318 (12.1%) | 2,093 (10.9%) | 0.04 | 1,468 (7.1%) | 1,206 (5.8%) | 0.05 | 8,654 (19.5%) | 8,706 (19.6%) | 0.00 | 12,440 (14.7%) | 12,005 (14.2%) |
| Gender - United | | | | | | | | | | | |
| ...Males; n (%) | 9,107 (47.5%) | 9,089 (47.4%) | 0.00 | 10,509 (50.6%) | 10,673 (51.4%) | -0.02 | 19,489 (43.9%) | 19,600 (44.2%) | -0.01 | 39,105 (46.4%) | 39,362 (46.7%) |
| ...Females; n (%) | 10,080 (52.5%) | 10,098 (52.6%) | 0.00 | 10,268 (49.4%) | 10,104 (48.6%) | 0.02 | 24,892 (56.1%) | 24,781 (55.8%) | 0.01 | 45,240 (53.6%) | 44,983 (53.3%) |
| Race | | | | | | | | | | | |
| ...White; n (%) | N/A | N/A | | N/A | N/A | | 38,069 (85.8%) | 37,846 (85.3%) | 0.01 | 38,069 (85.8%) | 37,846 (85.3%) |
| ...Black; n (%) | N/A | N/A | | N/A | N/A | | 3,578 (8.1%) | 3,789 (8.5%) | -0.01 | 3,578 (8.1%) | 3,789 (8.5%) |
| ...Asian; n (%) | N/A | N/A | | N/A | N/A | | 464 (1.0%) | 531 (1.2%) | -0.02 | 464 (1.0%) | 531 (1.2%) |
| ...Hispanic; n (%) | N/A | N/A | | N/A | N/A | | 837 (1.9%) | 801 (1.8%) | 0.01 | 837 (1.9%) | 801 (1.8%) |
| ...North American Native; n (%) | N/A | N/A | | N/A | N/A | | 179 (0.4%) | 177 (0.4%) | 0.00 | 179 (0.4%) | 177 (0.4%) |
| ...Other/Unknown; n (%) | N/A | N/A | | N/A | N/A | | 1,254 (2.8%) | 1,237 (2.8%) | 0.00 | 1,254 (2.8%) | 1,237 (2.8%) |
| Region - United (umping missing&other category with West) | | | | | | | | | | | |
| ...Northeast; n (%) | 1,677 (8.7%) | 1,736 (9.0%) | -0.01 | 3,838 (18.5%) | 3,945 (19.0%) | -0.01 | 6,816 (15.4%) | 6,961 (15.7%) | -0.01 | 12,331 (14.6%) | 12,642 (15.0%) |
| ...South; n (%) | 10,357 (54.0%) | 10,229 (53.3%) | 0.01 | 4,513 (21.7%) | 4,504 (21.7%) | 0.00 | 20,540 (46.3%) | 20,477 (46.1%) | 0.00 | 35,410 (42.0%) | 35,210 (41.7%) |
| ...Midwest; n (%) | 3,728 (19.4%) | 3,773 (19.7%) | -0.01 | 9,878 (47.5%) | 9,791 (47.1%) | 0.01 | 10,234 (23.1%) | 10,227 (23.0%) | 0.00 | 23,840 (28.3%) | 23,791 (28.2%) |
| ...West; n (%) | 3,425 (17.9%) | 3,449 (18.0%) | 0.00 | 2,326 (11.2%) | 2,314 (11.1%) | 0.00 | 6,791 (15.3%) | 6,716 (15.1%) | 0.01 | 12,542 (14.9%) | 12,479 (14.8%) |
| ...Unknown+missing; n (%) | N/A | N/A | #VALUE! | 222 (1.1%) | 223 (1.1%) | 0.00 | N/A | N/A | #VALUE! | 222 (1.1%) | 223 (1.1%) |
| CV Covariates | | | | | | | | | | | |
| Ischemic heart disease; n (%) | 5,701 (29.7%) | 5,722 (29.8%) | | 6,791 (32.7%) | 6,767 (32.6%) | | 13,769 (31.0%) | 13,776 (31.0%) | | 26,261 (31.1%) | 26,265 (31.1%) |
| Acute MI; n (%) | 291 (1.5%) | 290 (1.5%) | | 311 (1.5%) | 306 (1.5%) | | 554 (1.2%) | 535 (1.2%) | | 1,156 (1.4%) | 1,131 (1.3%) |
| ACS/unstable angina; n (%) | 370 (1.9%) | 389 (2.0%) | | 429 (2.1%) | 429 (2.1%) | | 814 (1.8%) | 739 (1.7%) | | 1,613 (1.9%) | 1,557 (1.8%) |
| Old MI; n (%) | 794 (4.1%) | 770 (4.0%) | | 403 (1.9%) | 428 (2.1%) | | 1,598 (3.6%) | 1,594 (3.6%) | | 2,795 (3.3%) | 2,792 (3.3%) |
| Stable angina; n (%) | 912 (4.8%) | 931 (4.9%) | | 730 (3.5%) | 742 (3.6%) | | 1,771 (4.0%) | 1,708 (3.8%) | | 3,413 (4.0%) | 3,381 (4.0%) |
| Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%) | 5,358 (27.9%) | 5,377 (28.0%) | | 6,498 (31.3%) | 6,468 (31.1%) | | 13,175 (29.7%) | 13,182 (29.7%) | | 25,031 (29.7%) | 25,027 (29.7%) |
| Other atherosclerosis with ICD10 ; n (%) | 184 (1.0%) | 201 (1.0%) | | 240 (1.2%) | 238 (1.1%) | | 683 (1.5%) | 756 (1.7%) | | 1,107 (1.3%) | 1,195 (1.4%) |
| Previous cardiac procedure (CABG or PTCA or Stent) ; n (%) | 168 (0.9%) | 173 (0.9%) | | 221 (1.1%) | 211 (1.0%) | | 300 (0.7%) | 233 (0.5%) | | 689 (0.8%) | 617 (0.7%) |
| History of CABG or PTCA; n (%) | 1,375 (7.2%) | 1,387 (7.2%) | | 840 (4.0%) | 825 (4.0%) | | 3,726 (8.4%) | 3,698 (8.3%) | | 5,941 (7.0%) | 5,910 (7.0%) |
| Any stroke; n (%) | 1,414 (7.4%) | 1,401 (7.3%) | | 1,494 (7.2%) | 1,500 (7.2%) | | 3,852 (8.7%) | 3,786 (8.5%) | | 6,760 (8.0%) | 6,687 (7.9%) |
| Ischemic stroke (w and w/o mention of cerebral infarction); n (%) | 1,392 (7.3%) | 1,390 (7.2%) | | 1,476 (7.1%) | 1,479 (7.1%) | | 3,816 (8.6%) | 3,753 (8.5%) | | 6,684 (7.9%) | 6,622 (7.9%) |
| Hemorrhagic stroke; n (%) | 38 (0.2%) | 31 (0.2%) | | 37 (0.2%) | 36 (0.2%) | | 80 (0.2%) | 62 (0.1%) | | 155 (0.2%) | 129 (0.2%) |
| TIA; n (%) | 328 (1.7%) | 326 (1.7%) | | 379 (1.8%) | 363 (1.7%) | | 848 (1.9%) | 769 (1.7%) | | 1,555 (1.8%) | 1,458 (1.7%) |
| Other cerebrovascular disease; n (%) | 355 (1.9%) | 330 (1.7%) | | 255 (1.2%) | 237 (1.1%) | | 883 (2.0%) | 895 (2.0%) | | 1,493 (1.8%) | 1,462 (1.7%) |
| Late effects of cerebrovascular disease; n (%) | 261 (1.4%) | 244 (1.3%) | | 142 (0.7%) | 150 (0.7%) | | 598 (1.3%) | 634 (1.4%) | | 1,001 (1.2%) | 1,028 (1.2%) |
| Cerebrovascular procedure; n (%) | 9 (0.0%) | 21 (0.1%) | | 24 (0.1%) | 24 (0.1%) | | 61 (0.1%) | 45 (0.1%) | | 094 (0.1%) | 090 (0.1%) |
| Heart failure (CHF); n (%) | 2,017 (10.5%) | 2,032 (10.6%) | | 1,594 (7.7%) | 1,572 (7.6%) | | 4,950 (11.2%) | 4,901 (11.0%) | | 8,561 (10.1%) | 8,505 (10.1%) |
| Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%) | 1,696 (8.8%) | 1,705 (8.9%) | | 1,697 (8.2%) | 1,671 (8.0%) | | 4,485 (10.1%) | 4,556 (10.3%) | | 7,878 (9.3%) | 7,932 (9.4%) |
| Atrial fibrillation; n (%) | 1,491 (7.8%) | 1,541 (8.0%) | | 1,240 (6.0%) | 1,237 (6.0%) | | 4,728 (10.7%) | 4,771 (10.8%) | | 7,459 (8.8%) | 7,549 (9.0%) |
| Other cardiac dysrhythmia; n (%) | 2,008 (10.5%) | 1,993 (10.4%) | | 1,498 (7.2%) | 1,470 (7.1%) | | 5,142 (11.6%) | 5,106 (11.5%) | | 8,648 (10.3%) | 8,569 (10.2%) |
| Cardiac conduction disorders; n (%) | 538 (2.8%) | 543 (2.8%) | | 411 (2.0%) | 425 (2.0%) | | 1,563 (3.5%) | 1,628 (3.7%) | | 2,512 (3.0%) | 2,596 (3.1%) |
| Other CVD; n (%) | 2,256 (11.8%) | 2,274 (11.9%) | | 2,290 (11.0%) | 2,252 (10.8%) | | 6,456 (14.5%) | 6,303 (14.2%) | | 11,002 (13.0%) | 10,829 (12.8%) |
| Diabetes-related complications | | | | | | | | | | | |
| Diabetic retinopathy; n (%) | 1,444 (7.5%) | 1,474 (7.7%) | | 989 (4.8%) | 1,022 (4.9%) | | 3,663 (8.3%) | 3,676 (8.3%) | | 6,096 (7.2%) | 6,172 (7.3%) |
| Diabetes with other ophthalmic manifestations; n (%) | 143 (0.7%) | 140 (0.7%) | | 678 (3.3%) | 726 (3.5%) | | 1,377 (3.1%) | 1,449 (3.3%) | | 2,198 (2.6%) | 2,315 (2.7%) |
| Retinal detachment, vitreous hemorrhage, vitrectomy; n (%) | 104 (0.5%) | 83 (0.4%) | | 102 (0.5%) | 71 (0.3%) | | 219 (0.5%) | 192 (0.4%) | | 425 (0.5%) | 346 (0.4%) |
| Retinal laser coagulation therapy; n (%) | 128 (0.7%) | 120 (0.6%) | | 149 (0.7%) | 137 (0.7%) | | 350 (0.8%) | 289 (0.7%) | | 627 (0.7%) | 546 (0.6%) |
| Occurrence of Diabetic Neuropathy ; n (%) | 4,593 (23.9%) | 4,623 (24.1%) | | 2,969 (14.3%) | 2,964 (14.3%) | | 10,346 (23.3%) | 10,291 (23.2%) | | 17,908 (21.2%) | 17,878 (21.2%) |
| Occurrence of diabetic nephropathy with ICD10 ; n (%) | 3,404 (17.7%) | 3,439 (17.9%) | | 1,655 (8.0%) | 1,662 (8.0%) | | 5,588 (12.6%) | 5,562 (12.5%) | | 10,647 (12.6%) | 10,663 (12.6%) |
| Hypoglycemia ; n (%) | 476 (2.5%) | 476 (2.5%) | | 606 (2.9%) | 625 (3.0%) | | 1,381 (3.1%) | 1,358 (3.1%) | | 2,463 (2.9%) | 2,459 (2.9%) |
| Hyperglycemia; n (%) | 754 (3.9%) | 747 (3.9%) | | 547 (2.6%) | 546 (2.6%) | | 1,711 (3.9%) | 1,673 (3.8%) | | 3,012 (3.6%) | 2,966 (3.5%) |
| Disorders of fluid electrolyte and acid-base balance; n (%) | 1,297 (6.8%) | 1,346 (7.0%) | | 986 (4.7%) | 950 (4.6%) | | 3,358 (7.6%) | 3,341 (7.5%) | | 5,641 (6.7%) | 5,637 (6.7%) |
| Diabetic ketoacidosis; n (%) | 25 (0.1%) | 21 (0.1%) | | 29 (0.1%) | 20 (0.1%) | | 61 (0.1%) | 53 (0.1%) | | 115 (0.1%) | 094 (0.1%) |
| Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%) | 94 (0.5%) | 95 (0.5%) | | 80 (0.4%) | 73 (0.4%) | | 194 (0.4%) | 193 (0.4%) | | 368 (0.4%) | 361 (0.4%) |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | |
|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|---------|
| Diabetes with peripheral circulatory disorders with | | | | | | | | | |
| ICD-10 ; n (%) | 1,565 (8.2%) | 1,519 (7.9%) | 831 (4.0%) | 871 (4.2%) | 3,179 (7.2%) | 3,210 (7.2%) | 5,575 (6.6%) | 5,600 (6.6%) | 0.00 |
| Diabetic Foot; n (%) | 499 (2.6%) | 494 (2.6%) | 490 (2.4%) | 483 (2.3%) | 1,340 (3.0%) | 1,361 (3.1%) | 2,329 (2.8%) | 2,338 (2.8%) | 0.00 |
| Gangrene; n (%) | 61 (0.3%) | 48 (0.3%) | 39 (0.2%) | 33 (0.2%) | 80 (0.2%) | 83 (0.2%) | 180 (0.2%) | 164 (0.2%) | 0.00 |
| Lower extremity amputation; n (%) | 173 (0.9%) | 146 (0.8%) | 75 (0.4%) | 69 (0.3%) | 230 (0.5%) | 228 (0.5%) | 478 (0.6%) | 443 (0.5%) | 0.01 |
| Osteomyelitis; n (%) | 136 (0.7%) | 110 (0.6%) | 127 (0.6%) | 119 (0.6%) | 259 (0.6%) | 225 (0.5%) | 522 (0.6%) | 454 (0.5%) | 0.01 |
| Skin infections; n (%) | 1,175 (6.1%) | 1,153 (6.0%) | 1,262 (6.1%) | 1,283 (6.2%) | 3,424 (7.7%) | 3,359 (7.6%) | 5,861 (6.9%) | 5,795 (6.9%) | 0.00 |
| Erectile dysfunction; n (%) | 561 (2.9%) | 589 (3.1%) | 532 (2.6%) | 525 (2.5%) | 1,286 (2.9%) | 1,306 (2.9%) | 2,379 (2.8%) | 2,420 (2.9%) | -0.01 |
| Diabetes with unspecified complication; n (%) | 1,183 (6.2%) | 1,212 (6.3%) | 1,013 (4.9%) | 998 (4.8%) | 2,448 (5.5%) | 2,456 (5.5%) | 4,644 (5.5%) | 4,666 (5.5%) | 0.00 |
| Diabetes mellitus without mention of complications; n (%) | 16,719 (87.1%) | 16,712 (87.1%) | 19,433 (93.5%) | 19,456 (93.6%) | 41,391 (93.3%) | 41,385 (93.2%) | 77,543 (91.9%) | 77,553 (91.9%) | 0.00 |
| Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%) | 18,326 (95.5%) | 18,285 (95.3%) | 18,379 (88.5%) | 18,392 (88.5%) | 43,029 (97.0%) | 43,046 (97.0%) | 79,734 (94.5%) | 79,723 (94.5%) | 0.00 |
| Hyperlipidemia; n (%) | 15,189 (79.2%) | 15,133 (78.9%) | 14,678 (70.6%) | 14,741 (70.9%) | 36,860 (83.1%) | 36,848 (83.0%) | 66,727 (79.1%) | 66,722 (79.1%) | 0.00 |
| Edema; n (%) | 1,701 (8.9%) | 1,712 (8.9%) | 1,292 (6.2%) | 1,286 (6.2%) | 4,774 (10.8%) | 4,790 (10.8%) | 7,767 (9.2%) | 7,788 (9.2%) | 0.00 |
| Renal Dysfunction (non-diabetic) ; n (%) | 4,574 (23.8%) | 4,607 (24.0%) | 2,981 (14.3%) | 2,999 (14.4%) | 9,976 (22.5%) | 9,939 (22.4%) | 17,531 (20.8%) | 17,545 (20.8%) | 0.00 |
| Occurrence of acute renal disease ; n (%) | 618 (3.2%) | 618 (3.2%) | 389 (1.9%) | 387 (1.9%) | 1,410 (3.2%) | 1,420 (3.2%) | 2,417 (2.9%) | 2,425 (2.9%) | 0.00 |
| Occurrence of chronic renal insufficiency; n (%) | 3,958 (20.6%) | 3,966 (20.7%) | 2,293 (11.0%) | 2,341 (11.3%) | 8,564 (19.3%) | 8,551 (19.3%) | 14,815 (17.6%) | 14,858 (17.6%) | 0.00 |
| Chronic kidney disease ; n (%) | 3,820 (19.9%) | 3,855 (20.1%) | 2,212 (10.6%) | 2,256 (10.9%) | 8,088 (18.2%) | 8,088 (18.2%) | 14,120 (16.7%) | 14,199 (16.8%) | 0.00 |
| CKD Stage 3-4; n (%) | 2,841 (14.8%) | 2,830 (14.7%) | 1,649 (7.9%) | 1,698 (8.2%) | 5,873 (13.2%) | 5,830 (13.1%) | 10,363 (12.3%) | 10,358 (12.3%) | 0.00 |
| Occurrence of hypertensive nephropathy; n (%) | 1,663 (8.7%) | 1,699 (8.9%) | 836 (4.0%) | 857 (4.1%) | 3,487 (7.9%) | 3,481 (7.8%) | 5,986 (7.1%) | 6,037 (7.2%) | 0.00 |
| Occurrence of miscellaneous renal insufficiency ; n (%) | 1,009 (5.3%) | 1,008 (5.3%) | 779 (3.7%) | 783 (3.8%) | 3,026 (6.8%) | 2,878 (6.5%) | 4,814 (5.7%) | 4,669 (5.5%) | 0.01 |
| Glaucoma or cataracts ; n (%) | 4,154 (21.7%) | 4,031 (21.0%) | 3,827 (18.4%) | 3,680 (17.7%) | 12,558 (28.3%) | 12,492 (28.1%) | 20,539 (24.4%) | 20,203 (24.0%) | 0.01 |
| Cellulitis or abscess of toe; n (%) | 330 (1.7%) | 296 (1.5%) | 221 (1.1%) | 210 (1.0%) | 682 (1.5%) | 667 (1.5%) | 1,233 (1.5%) | 1,173 (1.4%) | 0.01 |
| Foot ulcer; n (%) | 475 (2.5%) | 475 (2.5%) | 494 (2.4%) | 484 (2.3%) | 1,332 (3.0%) | 1,339 (3.0%) | 2,301 (2.7%) | 2,298 (2.7%) | 0.00 |
| Bladder stones; n (%) | 28 (0.1%) | 14 (0.1%) | 21 (0.1%) | 22 (0.1%) | 77 (0.2%) | 73 (0.2%) | 126 (0.1%) | 109 (0.1%) | 0.00 |
| Kidney stones; n (%) | 473 (2.5%) | 461 (2.4%) | 528 (2.5%) | 512 (2.5%) | 1,276 (2.9%) | 1,295 (2.9%) | 2,277 (2.7%) | 2,268 (2.7%) | 0.00 |
| Urinary tract infections (UTIs); n (%) | 1,744 (9.1%) | 1,711 (8.9%) | 1,375 (6.6%) | 1,356 (6.5%) | 5,473 (12.3%) | 5,479 (12.3%) | 8,592 (10.2%) | 8,546 (10.1%) | 0.00 |
| Dipstick urinalysis; n (%) | 7,240 (37.7%) | 6,927 (36.1%) | 7,253 (34.9%) | 6,731 (32.4%) | 18,427 (41.5%) | 17,759 (40.0%) | 32,920 (39.0%) | 31,417 (37.2%) | 0.04 |
| Non-dipstick urinalysis; n (%) | 8,574 (44.7%) | 8,615 (44.9%) | 7,423 (35.7%) | 7,462 (35.9%) | 20,541 (46.3%) | 20,649 (46.5%) | 36,538 (43.3%) | 36,726 (43.5%) | 0.00 |
| Urine function test; n (%) | 478 (2.5%) | 464 (2.4%) | 532 (2.6%) | 503 (2.4%) | 1,674 (3.8%) | 1,519 (3.4%) | 2,684 (3.2%) | 2,486 (2.9%) | 0.02 |
| Cytology; n (%) | 131 (0.7%) | 127 (0.7%) | 201 (1.0%) | 179 (0.9%) | 443 (1.0%) | 401 (0.9%) | 775 (0.9%) | 707 (0.8%) | 0.01 |
| Cystos; n (%) | 230 (1.2%) | 238 (1.2%) | 267 (1.3%) | 253 (1.2%) | 726 (1.6%) | 653 (1.5%) | 1,223 (1.4%) | 1,144 (1.4%) | 0.00 |
| Other Covariates | | | | | | | | | |
| Liver disease; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 000 (0.0%) | 000 (0.0%) | #DIV/0! |
| Osteoarthritis; n (%) | 3,745 (19.5%) | 3,782 (19.7%) | 3,160 (15.2%) | 3,192 (15.4%) | 10,957 (24.7%) | 10,991 (24.8%) | 17,862 (21.2%) | 17,965 (21.3%) | 0.00 |
| Other arthritis, arthropathies and musculoskeletal pain; n (%) | | | | | | | | | |
| Dorsopathies; n (%) | 7,765 (40.5%) | 7,671 (40.0%) | 7,650 (36.8%) | 7,628 (36.7%) | 21,066 (47.5%) | 20,955 (47.2%) | 36,481 (43.3%) | 36,254 (43.0%) | 0.01 |
| Fractures; n (%) | 5,026 (26.2%) | 5,009 (26.1%) | 4,446 (21.4%) | 4,472 (21.5%) | 13,404 (30.2%) | 13,332 (30.0%) | 22,876 (27.1%) | 22,813 (27.0%) | 0.00 |
| Falls ; n (%) | 523 (2.7%) | 543 (2.8%) | 524 (2.5%) | 524 (2.5%) | 1,530 (3.4%) | 1,562 (3.5%) | 2,581 (3.1%) | 2,629 (3.1%) | 0.00 |
| Osteoporosis; n (%) | 600 (3.1%) | 605 (3.2%) | 182 (0.9%) | 183 (0.9%) | 1,506 (3.4%) | 1,482 (3.3%) | 2,288 (2.7%) | 2,270 (2.7%) | 0.00 |
| Hypothyroidism; n (%) | 737 (3.8%) | 786 (4.1%) | 624 (3.0%) | 607 (2.9%) | 2,931 (6.6%) | 2,880 (6.5%) | 4,292 (5.1%) | 4,273 (5.1%) | 0.00 |
| Hyperthyroidism; n (%) | 191 (1.0%) | 125 (0.7%) | 157 (0.8%) | 104 (0.5%) | 523 (1.2%) | 412 (0.9%) | 871 (1.0%) | 641 (0.8%) | -0.02 |
| Hypothyroidism ; n (%) | 3,602 (18.8%) | 3,737 (19.5%) | 2,944 (14.2%) | 2,959 (14.2%) | 7,649 (17.2%) | 7,701 (17.4%) | 14,195 (16.8%) | 14,397 (17.1%) | 0.01 |
| Other disorders of thyroid gland ; n (%) | 1,019 (5.3%) | 969 (5.1%) | 999 (4.8%) | 991 (4.8%) | 2,714 (6.1%) | 2,573 (5.8%) | 4,732 (5.6%) | 4,533 (5.4%) | 0.01 |
| Depression; n (%) | 2,008 (10.5%) | 1,965 (10.2%) | 1,630 (7.8%) | 1,611 (7.8%) | 5,365 (12.1%) | 5,264 (11.9%) | 9,003 (10.7%) | 8,840 (10.5%) | 0.01 |
| Anxiety; n (%) | 1,752 (9.1%) | 1,698 (8.8%) | 1,109 (5.3%) | 1,066 (5.1%) | 3,825 (8.6%) | 3,722 (8.4%) | 6,686 (7.9%) | 6,486 (7.7%) | 0.01 |
| Sleep_Disorder; n (%) | 2,068 (10.8%) | 2,062 (10.7%) | 3,430 (16.5%) | 3,424 (16.5%) | 5,922 (13.3%) | 5,843 (13.2%) | 11,420 (13.5%) | 11,329 (13.4%) | 0.00 |
| Dementia; n (%) | 389 (2.0%) | 405 (2.1%) | 209 (1.0%) | 211 (1.0%) | 1,458 (3.3%) | 1,482 (3.3%) | 2,056 (2.4%) | 2,098 (2.5%) | -0.01 |
| Delirium; n (%) | 141 (0.7%) | 145 (0.8%) | 89 (0.4%) | 91 (0.4%) | 470 (1.1%) | 482 (1.1%) | 700 (0.8%) | 718 (0.9%) | -0.01 |
| Psychosis; n (%) | 140 (0.7%) | 131 (0.7%) | 82 (0.4%) | 80 (0.4%) | 430 (1.0%) | 410 (0.9%) | 652 (0.8%) | 621 (0.7%) | 0.01 |
| Obesity; n (%) | 6,359 (33.1%) | 6,321 (32.9%) | 4,461 (21.5%) | 4,453 (21.4%) | 11,476 (25.9%) | 11,510 (25.9%) | 22,296 (26.4%) | 22,284 (26.4%) | 0.00 |
| Overweight; n (%) | 860 (4.5%) | 830 (4.3%) | 356 (1.7%) | 357 (1.7%) | 1,167 (2.6%) | 1,226 (2.8%) | 2,383 (2.8%) | 2,413 (2.9%) | -0.01 |
| Smoking; n (%) | 2,270 (11.8%) | 2,211 (11.5%) | 979 (4.7%) | 971 (4.7%) | 5,447 (12.3%) | 5,371 (12.1%) | 8,696 (10.3%) | 8,553 (10.1%) | 0.01 |
| Alcohol abuse or dependence; n (%) | 88 (0.5%) | 85 (0.4%) | 53 (0.3%) | 57 (0.3%) | 167 (0.4%) | 157 (0.4%) | 308 (0.4%) | 299 (0.4%) | 0.00 |
| Drug abuse or dependence; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 000 (0.0%) | 000 (0.0%) | #DIV/0! |
| COPD; n (%) | 1,967 (10.3%) | 1,937 (10.1%) | 1,281 (6.2%) | 1,259 (6.1%) | 5,022 (11.3%) | 4,898 (11.0%) | 8,270 (9.8%) | 8,094 (9.6%) | 0.01 |
| Asthma; n (%) | 1,425 (7.4%) | 1,397 (7.3%) | 1,264 (6.1%) | 1,216 (5.9%) | 3,583 (8.1%) | 3,478 (7.8%) | 6,272 (7.4%) | 6,091 (7.2%) | 0.01 |
| Obstructive sleep apnea; n (%) | 3,445 (18.0%) | 3,467 (18.1%) | 3,570 (17.2%) | 3,587 (17.3%) | 6,167 (13.9%) | 6,100 (13.7%) | 13,182 (15.6%) | 13,154 (15.6%) | 0.00 |
| Pneumonia; n (%) | 431 (2.2%) | 430 (2.2%) | 407 (2.0%) | 407 (2.0%) | 1,192 (2.7%) | 1,168 (2.6%) | 2,030 (2.4%) | 2,005 (2.4%) | 0.00 |
| Imaging; n (%) | 20 (0.1%) | 26 (0.1%) | 11 (0.1%) | 14 (0.1%) | 46 (0.1%) | 50 (0.1%) | 77 (0.1%) | 90 (0.1%) | 0.00 |
| Diabetes Medications | | | | | | | | | |
| DM Medications - AGIs; n (%) | 94 (0.5%) | 99 (0.5%) | 78 (0.4%) | 81 (0.4%) | 273 (0.6%) | 253 (0.6%) | 445 (0.5%) | 433 (0.5%) | 0.00 |
| DM Medications - Glitazones; n (%) | 2,266 (11.8%) | 2,253 (11.7%) | 3,295 (15.9%) | 3,271 (15.7%) | 4,782 (10.8%) | 4,697 (10.6%) | 10,343 (12.3%) | 10,221 (12.1%) | 0.01 |
| DM Medications - Insulin; n (%) | 3,103 (16.2%) | 3,311 (17.3%) | 3,209 (15.4%) | 3,403 (16.4%) | 8,242 (18.6%) | 8,597 (19.4%) | 14,554 (17.3%) | 15,311 (18.2%) | -0.02 |
| DM Medications - Meglitinides; n (%) | 243 (1.3%) | 216 (1.1%) | 373 (1.8%) | 360 (1.7%) | 688 (1.6%) | 693 (1.6%) | 1,304 (1.5%) | 1,269 (1.5%) | 0.00 |
| DM Medications - Metformin; n (%) | 12,397 (64.6%) | 12,229 (63.7%) | 14,006 (67.4%) | 13,878 (66.8%) | 28,993 (65.3%) | 28,918 (65.2%) | 55,396 (65.7%) | 55,025 (65.2%) | 0.01 |
| Concomitant initiation or current use of SGLT2i; n (%) | | | | | | | | | |
| Concomitant initiation or current use of AGIs; n (%) | 1,051 (5.5%) | 1,051 (5.5%) | 956 (4.6%) | 991 (4.8%) | 1,726 (3.9%) | 1,657 (3.7%) | 3,733 (4.4%) | 3,699 (4.4%) | 0.00 |
| Concomitant initiation or current use of Glitazones; n (%) | 63 (0.3%) | 67 (0.3%) | 49 (0.2%) | 48 (0.2%) | 176 (0.4%) | 171 (0.4%) | 288 (0.3%) | 286 (0.3%) | 0.00 |
| Concomitant initiation or current use of 2nd Generation SUs; n (%) | | | | | | | | | |
| | 1,682 (8.8%) | 1,642 (8.6%) | 2,421 (11.7%) | 2,382 (11.5%) | 3,540 (8.0%) | 3,503 (7.9%) | 7,643 (9.1%) | 7,527 (8.9%) | 0.01 |
| | 5,856 (30.5%) | 5,716 (29.8%) | 6,217 (29.9%) | 6,177 (29.7%) | 14,954 (33.7%) | 14,751 (33.2%) | 27,027 (32.0%) | 26,644 (31.6%) | 0.01 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | |
|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|---------|
| Concomitant initiation or current use of Insulin; n (%) | 1,846 (9.6%) | 1,981 (10.3%) | 1,893 (9.1%) | 2,025 (9.7%) | 4,918 (11.1%) | 5,173 (11.7%) | 8,657 (10.3%) | 9,179 (10.9%) | -0.02 |
| Concomitant initiation or current use of Meglitinides; n (%) | 164 (0.9%) | 137 (0.7%) | 268 (1.3%) | 251 (1.2%) | 485 (1.1%) | 472 (1.1%) | 917 (1.1%) | 860 (1.0%) | 0.01 |
| Concomitant initiation or current use of Metformin; n (%) | 10,067 (52.5%) | 9,937 (51.8%) | 11,259 (54.2%) | 11,194 (53.9%) | 23,633 (53.3%) | 23,628 (53.2%) | 44,959 (53.3%) | 44,759 (53.1%) | 0.00 |
| Past use of SGLT2i ; n (%) | 425 (2.2%) | 406 (2.1%) | 357 (1.7%) | 347 (1.7%) | 788 (1.8%) | 740 (1.7%) | 1,570 (1.9%) | 1,493 (1.8%) | 0.01 |
| Past use of AGIs ; n (%) | 31 (0.2%) | 32 (0.2%) | 29 (0.1%) | 33 (0.2%) | 97 (0.2%) | 82 (0.2%) | 157 (0.2%) | 147 (0.2%) | 0.00 |
| Past use of Glitazones ; n (%) | 584 (3.0%) | 611 (3.2%) | 874 (4.2%) | 889 (4.3%) | 1,242 (2.8%) | 1,194 (2.7%) | 2,700 (3.2%) | 2,694 (3.2%) | 0.00 |
| Past use of 2nd Generation SUs; n (%) | 1,529 (8.0%) | 1,517 (7.9%) | 1,708 (8.2%) | 1,699 (8.2%) | 3,958 (8.9%) | 3,827 (8.6%) | 7,195 (8.5%) | 7,043 (8.4%) | 0.00 |
| Past use of Insulin ; n (%) | 1,257 (6.6%) | 1,330 (6.9%) | 1,316 (6.3%) | 1,378 (6.6%) | 3,325 (7.5%) | 3,424 (7.7%) | 5,898 (7.0%) | 6,132 (7.3%) | -0.01 |
| Past use of Meglitinides ; n (%) | 79 (0.4%) | 79 (0.4%) | 105 (0.5%) | 109 (0.5%) | 203 (0.5%) | 221 (0.5%) | 387 (0.5%) | 409 (0.5%) | 0.00 |
| Past use of metformin (final) ; n (%) | 2,330 (12.1%) | 2,292 (11.9%) | 2,747 (13.2%) | 2,684 (12.9%) | 5,360 (12.1%) | 5,290 (11.9%) | 10,437 (12.4%) | 10,266 (12.2%) | 0.01 |
| Other Medications | | | | | | | | | |
| Use of ACE inhibitors; n (%) | 8,661 (45.1%) | 8,617 (44.9%) | 9,287 (44.7%) | 9,226 (44.4%) | 19,748 (44.5%) | 19,720 (44.4%) | 37,696 (44.7%) | 37,563 (44.5%) | 0.00 |
| Use of ARBs; n (%) | 6,420 (33.5%) | 6,450 (33.6%) | 7,474 (36.0%) | 7,522 (36.2%) | 15,578 (35.1%) | 15,693 (35.4%) | 29,472 (34.9%) | 29,665 (35.2%) | -0.01 |
| Use of Loop Diuretics - United; n (%) | 3,398 (17.7%) | 3,483 (18.2%) | 3,539 (17.0%) | 3,497 (16.8%) | 9,714 (21.9%) | 9,727 (21.9%) | 16,651 (19.7%) | 16,707 (19.8%) | 0.00 |
| Use of other diuretics- United; n (%) | 863 (4.5%) | 886 (4.6%) | 968 (4.7%) | 942 (4.5%) | 2,181 (4.9%) | 2,151 (4.8%) | 4,012 (4.8%) | 3,979 (4.7%) | 0.00 |
| Use of nitrates-United; n (%) | 1,373 (7.2%) | 1,383 (7.2%) | 1,513 (7.3%) | 1,556 (7.5%) | 3,530 (8.0%) | 3,518 (7.9%) | 6,416 (7.6%) | 6,457 (7.7%) | 0.00 |
| Use of other hypertension drugs; n (%) | 1,516 (7.9%) | 1,494 (7.8%) | 1,480 (7.1%) | 1,479 (7.1%) | 3,871 (8.7%) | 3,814 (8.6%) | 6,867 (8.1%) | 6,787 (8.0%) | 0.00 |
| Use of digoxin - United; n (%) | 310 (1.6%) | 320 (1.7%) | 388 (1.9%) | 392 (1.9%) | 1,018 (2.3%) | 1,020 (2.3%) | 1,716 (2.0%) | 1,732 (2.1%) | -0.01 |
| Use of Anti-arrhythmics; n (%) | 345 (1.8%) | 337 (1.8%) | 339 (1.6%) | 355 (1.7%) | 954 (2.1%) | 969 (2.2%) | 1,638 (1.9%) | 1,661 (2.0%) | -0.01 |
| Use of COPD/asthma meds- United; n (%) | 3,408 (17.8%) | 3,324 (17.3%) | 3,810 (18.3%) | 3,727 (17.9%) | 8,701 (19.6%) | 8,565 (19.3%) | 15,919 (18.9%) | 15,616 (18.5%) | 0.01 |
| Use of statins; n (%) | 13,833 (72.1%) | 13,840 (72.1%) | 14,918 (71.8%) | 14,906 (71.7%) | 32,249 (72.7%) | 32,353 (72.9%) | 61,000 (72.3%) | 61,099 (72.4%) | 0.00 |
| Use of other lipid-lowering drugs; n (%) | 2,758 (14.4%) | 2,721 (14.2%) | 3,849 (18.5%) | 3,863 (18.6%) | 6,812 (15.3%) | 6,760 (15.2%) | 13,419 (15.9%) | 13,344 (15.8%) | 0.00 |
| Use of antiplatelet agents; n (%) | 2,967 (15.5%) | 2,944 (15.3%) | 4,046 (19.5%) | 3,989 (19.2%) | 6,933 (15.6%) | 6,970 (15.7%) | 13,946 (16.5%) | 13,903 (16.5%) | 0.00 |
| Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%) | 1,430 (7.5%) | 1,453 (7.6%) | 1,380 (6.6%) | 1,370 (6.6%) | 4,150 (9.4%) | 4,252 (9.6%) | 6,960 (8.3%) | 7,075 (8.4%) | 0.00 |
| Use of heparin and other low-molecular weight heparins; n (%) | 103 (0.5%) | 103 (0.5%) | 0 (0.0%) | 1 (0.0%) | 207 (0.5%) | 206 (0.5%) | 310 (0.4%) | 310 (0.4%) | 0.00 |
| Use of NSAIDs; n (%) | 3,375 (17.6%) | 3,404 (17.7%) | 3,669 (17.7%) | 3,588 (17.3%) | 7,998 (18.0%) | 7,985 (18.0%) | 15,042 (17.8%) | 14,977 (17.8%) | 0.00 |
| Use of oral corticosteroids; n (%) | 3,235 (16.9%) | 3,239 (16.9%) | 3,346 (16.1%) | 3,257 (15.7%) | 8,099 (18.2%) | 7,995 (18.0%) | 14,680 (17.4%) | 14,491 (17.2%) | 0.01 |
| Use of bisphosphonate (United); n (%) | 303 (1.6%) | 349 (1.8%) | 324 (1.6%) | 308 (1.5%) | 1,096 (2.5%) | 1,047 (2.4%) | 1,723 (2.0%) | 1,704 (2.0%) | 0.00 |
| Use of opioids- United; n (%) | 5,625 (29.3%) | 5,525 (28.8%) | 6,002 (28.9%) | 6,018 (29.0%) | 13,107 (29.5%) | 13,033 (29.4%) | 24,734 (29.3%) | 24,576 (29.1%) | 0.00 |
| Use of antidepressants; n (%) | 6,011 (31.3%) | 5,924 (30.9%) | 6,205 (29.9%) | 6,074 (29.2%) | 14,221 (32.0%) | 14,173 (31.9%) | 26,437 (31.3%) | 26,171 (31.0%) | 0.01 |
| Use of antipsychotics; n (%) | 460 (2.4%) | 443 (2.3%) | 365 (1.8%) | 365 (1.8%) | 1,104 (2.5%) | 1,044 (2.4%) | 1,930 (2.3%) | 1,852 (2.2%) | 0.01 |
| Use of anticonvulsants; n (%) | 4,060 (21.2%) | 3,973 (20.7%) | 3,106 (14.9%) | 3,129 (15.1%) | 8,847 (19.9%) | 8,786 (19.8%) | 16,013 (19.0%) | 15,888 (18.8%) | 0.01 |
| Use of lithium- United; n (%) | 24 (0.1%) | 22 (0.1%) | 37 (0.2%) | 27 (0.1%) | 66 (0.1%) | 55 (0.1%) | 127 (0.2%) | 104 (0.1%) | 0.03 |
| Use of Benzos- United; n (%) | 2,251 (11.7%) | 2,238 (11.7%) | 2,514 (12.1%) | 2,553 (12.3%) | 4,924 (11.1%) | 4,945 (11.1%) | 9,689 (11.5%) | 9,736 (11.5%) | 0.00 |
| Use of anxiolytics/hypnotics- United; n (%) | 1,429 (7.4%) | 1,386 (7.2%) | 1,747 (8.4%) | 1,702 (8.2%) | 3,365 (7.6%) | 3,365 (7.6%) | 6,541 (7.8%) | 6,453 (7.7%) | 0.00 |
| Use of dementia meds- United; n (%) | 186 (1.0%) | 205 (1.1%) | 153 (0.7%) | 146 (0.7%) | 895 (2.0%) | 917 (2.1%) | 1,234 (1.5%) | 1,268 (1.5%) | 0.00 |
| Use of antiparkinsonian meds- United; n (%) | 664 (3.5%) | 666 (3.5%) | 630 (3.0%) | 638 (3.1%) | 1,810 (4.1%) | 1,794 (4.0%) | 3,104 (3.7%) | 3,098 (3.7%) | 0.00 |
| Any use of pramlintide; n (%) | 2 (0.0%) | 5 (0.0%) | 8 (0.0%) | 25 (0.1%) | 9 (0.0%) | 16 (0.0%) | 019 (0.0%) | 046 (0.1%) | -0.04 |
| Any use of 1st generation sulfonylureas; n (%) | 4 (0.0%) | 0 (0.0%) | 1 (0.0%) | 1 (0.0%) | 6 (0.0%) | 4 (0.0%) | 011 (0.0%) | 005 (0.0%) | 0.00 |
| Entresto (sacubitril/valsartan); n (%) | 50 (0.3%) | 47 (0.2%) | 18 (0.1%) | 13 (0.1%) | 44 (0.1%) | 27 (0.1%) | 112 (0.1%) | 087 (0.1%) | 0.00 |
| Initiation as monotherapy ; n (%) | 1,829 (9.5%) | 0 (0.0%) | 1,585 (7.6%) | 0 (0.0%) | 3,010 (6.8%) | 0 (0.0%) | 6,424 (7.6%) | #VALUE! | #VALUE! |
| Labs | | | | | | | 39,964 | 39,964 | |
| Lab values- HbA1c (%); n (%) | 7,630 (39.8%) | 7,216 (37.6%) | 1,331 (6.4%) | 1,167 (5.6%) | N/A | N/A | 8,961 (22.4%) | 8,383 (21.0%) | 0.03 |
| Lab values- HbA1c (%) (within 3 months); n (%) | 6,032 (31.4%) | 5,538 (28.9%) | 1,052 (5.1%) | 916 (4.4%) | N/A | N/A | 7,084 (17.7%) | 6,454 (16.1%) | 0.04 |
| Lab values- HbA1c (%) (within 6 months); n (%) | 7,630 (39.8%) | 7,216 (37.6%) | 1,331 (6.4%) | 1,167 (5.6%) | N/A | N/A | 8,961 (22.4%) | 8,383 (21.0%) | 0.03 |
| Lab values- BNP; n (%) | 211 (1.1%) | 206 (1.1%) | 25 (0.1%) | 34 (0.2%) | N/A | N/A | 236 (0.6%) | 240 (0.6%) | 0.00 |
| Lab values- BNP (within 3 months); n (%) | 117 (0.6%) | 121 (0.6%) | 14 (0.1%) | 28 (0.1%) | N/A | N/A | 131 (0.3%) | 149 (0.4%) | -0.02 |
| Lab values- BNP (within 6 months); n (%) | 211 (1.1%) | 206 (1.1%) | 25 (0.1%) | 34 (0.2%) | N/A | N/A | 236 (0.6%) | 240 (0.6%) | 0.00 |
| Lab values- BUN (mg/dl); n (%) | 7,901 (41.2%) | 7,376 (38.4%) | 1,341 (6.5%) | 1,179 (5.7%) | N/A | N/A | 9,242 (23.1%) | 8,555 (21.4%) | 0.04 |
| Lab values- BUN (mg/dl) (within 3 months); n (%) | 6,155 (32.1%) | 5,577 (29.1%) | 1,038 (5.0%) | 901 (4.3%) | N/A | N/A | 7,193 (18.0%) | 6,478 (16.2%) | 0.05 |
| Lab values- BUN (mg/dl) (within 6 months); n (%) | 7,901 (41.2%) | 7,376 (38.4%) | 1,341 (6.5%) | 1,179 (5.7%) | N/A | N/A | 9,242 (23.1%) | 8,555 (21.4%) | 0.04 |
| Lab values- Creatinine (mg/dl) ; n (%) | 8,092 (42.2%) | 7,583 (39.5%) | 1,405 (6.8%) | 1,228 (5.9%) | N/A | N/A | 9,497 (23.8%) | 8,811 (22.0%) | 0.04 |
| Lab values- Creatinine (mg/dl) (within 3 months); n (%) | 6,325 (33.0%) | 5,734 (29.9%) | 1,089 (5.2%) | 933 (4.5%) | N/A | N/A | 7,414 (18.6%) | 6,667 (16.7%) | 0.05 |
| Lab values- Creatinine (mg/dl) (within 6 months); n (%) | 8,092 (42.2%) | 7,583 (39.5%) | 1,405 (6.8%) | 1,228 (5.9%) | N/A | N/A | 9,497 (23.8%) | 8,811 (22.0%) | 0.04 |
| Lab values- HDL level (mg/dl); n (%) | 6,566 (34.2%) | 6,095 (31.8%) | 1,190 (5.7%) | 1,025 (4.9%) | N/A | N/A | 7,756 (19.4%) | 7,120 (17.8%) | 0.04 |
| Lab values- HDL level (mg/dl) (within 3 months); n (%) | 4,811 (25.1%) | 4,342 (22.6%) | 876 (4.2%) | 751 (3.6%) | N/A | N/A | 5,687 (14.2%) | 5,093 (12.7%) | 0.04 |
| Lab values- HDL level (mg/dl) (within 6 months); n (%) | 6,566 (34.2%) | 6,095 (31.8%) | 1,190 (5.7%) | 1,025 (4.9%) | N/A | N/A | 7,756 (19.4%) | 7,120 (17.8%) | 0.04 |
| Lab values- LDL level (mg/dl); n (%) | 6,757 (35.2%) | 6,299 (32.8%) | 1,235 (5.9%) | 1,085 (5.2%) | N/A | N/A | 7,992 (20.0%) | 7,384 (18.5%) | 0.04 |
| Lab values- LDL level (mg/dl) (within 3 months); n (%) | 4,956 (25.8%) | 4,495 (23.4%) | 911 (4.4%) | 789 (3.8%) | N/A | N/A | 5,867 (14.7%) | 5,284 (13.2%) | 0.04 |
| Lab values- LDL level (mg/dl) (within 6 months); n (%) | 6,757 (35.2%) | 6,299 (32.8%) | 1,235 (5.9%) | 1,085 (5.2%) | N/A | N/A | 7,992 (20.0%) | 7,384 (18.5%) | 0.04 |
| Lab values- NT-proBNP; n (%) | 36 (0.2%) | 35 (0.2%) | 3 (0.0%) | 2 (0.0%) | N/A | N/A | 39 (0.1%) | 0 (0.1%) | - |
| Lab values- NT-proBNP (within 3 months); n (%) | 21 (0.1%) | 22 (0.1%) | 3 (0.0%) | 0 (0.0%) | N/A | N/A | 24 (0.1%) | 0 (0.1%) | - |
| Lab values- NT-proBNP (within 6 months); n (%) | 36 (0.2%) | 35 (0.2%) | 3 (0.0%) | 2 (0.0%) | N/A | N/A | 39 (0.1%) | 37 (0.1%) | - |
| Lab values- Total cholesterol (mg/dl) ; n (%) | 6,680 (34.8%) | 6,217 (32.4%) | 1,209 (5.8%) | 1,039 (5.0%) | N/A | N/A | 7,889 (19.7%) | 7,256 (18.2%) | 0.04 |
| Lab values- Total cholesterol (mg/dl) (within 3 months); n (%) | 4,901 (25.5%) | 4,436 (23.1%) | 892 (4.3%) | 761 (3.7%) | N/A | N/A | 5,793 (14.5%) | 5,197 (13.0%) | 0.04 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|---|-------------------------|-------------------------|-------|-------------------------|-------------------------|-------|-------------------|-------------------|---------|--------------------|------------------|---------|
| Lab values- Total cholesterol (mg/dl) (within 6 months); n (%) | 6,680 (34.8%) | 6,217 (32.4%) | | 1,209 (5.8%) | 1,039 (5.0%) | | N/A | N/A | | 7,889 (19.7%) | 7,256 (18.2%) | 0.04 |
| Lab values- Triglyceride level (mg/dl); n (%) | 6,635 (34.6%) | 6,161 (32.1%) | | 1,197 (5.8%) | 1,020 (4.9%) | | N/A | N/A | | 7,832 (19.6%) | 7,181 (18.0%) | 0.04 |
| Lab values- Triglyceride level (mg/dl) (within 3 months); n (%) | 4,872 (25.4%) | 4,399 (22.9%) | | 885 (4.3%) | 747 (3.6%) | | N/A | N/A | | 5,757 (14.4%) | 5,146 (12.9%) | 0.04 |
| Lab values- Triglyceride level (mg/dl) (within 6 months); n (%) | 6,635 (34.6%) | 6,161 (32.1%) | | 1,197 (5.8%) | 1,020 (4.9%) | | N/A | N/A | | 7,832 (19.6%) | 7,181 (18.0%) | 0.04 |
| Lab result number- HbA1c (%) mean (only 2 to 20 included) | 7,607 | 7,179 | | 1,263 | 1,104 | | N/A | N/A | | 8,870 | 8,283 | |
| ...mean (sd) | 8.05 (1.64) | 8.03 (1.73) | 0.01 | 8.02 (1.62) | 8.03 (1.74) | -0.01 | N/A | N/A | #VALUE! | 8.05 (1.64) | 8.03 (1.73) | 0.01 |
| ...median [IQR] | 7.70 [6.95, 8.80] | 7.70 [6.80, 8.93] | 0.00 | 7.70 [6.90, 8.80] | 7.70 [6.80, 8.94] | 0.00 | N/A | N/A | #VALUE! | 7.70 (1.64) | 7.70 (1.73) | 0.00 |
| ...Missing; n (%) | 11,580 (60.4%) | 12,008 (62.6%) | -0.05 | 19,514 (93.9%) | 19,673 (94.7%) | -0.03 | N/A | N/A | #VALUE! | 31,094 (77.8%) | 31,681 (79.3%) | -0.04 |
| Lab result number- BNP mean | 211 | 206 | | 25 | 34 | | N/A | N/A | | 236 | 240 | |
| ...mean (sd) | 178.05 (453.45) | 112.46 (210.39) | 0.19 | 11,349.77 (55,969.06) | 98.46 (169.53) | 0.28 | N/A | N/A | #VALUE! | 1361.49 (17968.03) | 110.48 (205.64) | 0.10 |
| ...median [IQR] | 79.90 [31.80, 158.50] | 44.20 [21.62, 112.70] | 0.10 | 72.00 [34.50, 293.25] | 44.35 [16.25, 119.12] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 18,976 (98.9%) | 18,981 (98.9%) | 0.00 | 20,752 (99.9%) | 20,743 (99.8%) | 0.03 | N/A | N/A | #VALUE! | 39,728 (99.4%) | 39,724 (99.4%) | 0.00 |
| Lab result number- BUN (mg/dl) mean | 7,901 | 7,376 | | 1,341 | 1,179 | | N/A | N/A | | 9,242 | 8,555 | |
| ...mean (sd) | 19.20 (8.24) | 19.56 (8.24) | -0.04 | 424.78 (7,460.56) | 689.04 (11,932.92) | -0.03 | N/A | N/A | #VALUE! | 78.05 (2841.27) | 111.82 (4428.80) | -0.01 |
| ...median [IQR] | 17.40 [14.00, 22.00] | 18.00 [14.00, 23.00] | -0.07 | 17.00 [13.37, 21.00] | 18.00 [14.25, 22.00] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 11,286 (58.8%) | 11,811 (61.6%) | -0.06 | 19,436 (93.5%) | 19,598 (94.3%) | -0.03 | N/A | N/A | #VALUE! | 30,722 (76.9%) | 31,409 (78.6%) | -0.04 |
| Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) | 8,029 | 7,538 | | 1,288 | 1,121 | | N/A | N/A | | 9,317 | 8,659 | |
| ...mean (sd) | 1.06 (0.41) | 1.04 (0.37) | 0.05 | 1.02 (0.38) | 1.01 (0.32) | 0.03 | N/A | N/A | #VALUE! | 1.05 (0.41) | 1.04 (0.36) | 0.03 |
| ...median [IQR] | 0.97 [0.80, 1.21] | 0.96 [0.80, 1.20] | 0.03 | 0.96 [0.79, 1.12] | 0.96 [0.80, 1.14] | 0.00 | N/A | N/A | #VALUE! | 0.97 (0.41) | 0.96 (0.36) | 0.03 |
| ...Missing; n (%) | 11,158 (58.2%) | 11,649 (60.7%) | -0.05 | 19,489 (93.8%) | 19,656 (94.6%) | -0.03 | N/A | N/A | #VALUE! | 30,647 (76.7%) | 31,305 (78.3%) | -0.04 |
| Lab result number- HDL level (mg/dl) mean (only <=5000 included) | 6,566 | 6,095 | | 1,186 | 1,021 | | N/A | N/A | | 7,752 | 7,116 | |
| ...mean (sd) | 46.32 (13.75) | 45.91 (13.13) | 0.03 | 45.33 (15.96) | 44.46 (13.85) | 0.06 | N/A | N/A | #VALUE! | 46.17 (14.11) | 45.70 (13.24) | 0.03 |
| ...median [IQR] | 44.00 [37.00, 53.50] | 44.00 [37.00, 53.00] | 0.00 | 44.00 [36.00, 53.00] | 43.00 [36.00, 52.00] | 0.07 | N/A | N/A | #VALUE! | 44.00 (14.11) | 43.86 (13.24) | 0.01 |
| ...Missing; n (%) | 12,621 (65.8%) | 13,092 (68.2%) | -0.05 | 19,591 (94.3%) | 19,756 (95.1%) | -0.04 | N/A | N/A | #VALUE! | 32,212 (80.6%) | 32,848 (82.2%) | -0.04 |
| Lab result number- LDL level (mg/dl) mean (only <=5000 included) | 6,629 | 6,170 | | 1,149 | 949 | | N/A | N/A | | 7,778 | 7,119 | |
| ...mean (sd) | 85.21 (38.16) | 81.93 (36.98) | 0.09 | 84.96 (41.84) | 83.77 (40.06) | 0.03 | N/A | N/A | #VALUE! | 85.17 (38.73) | 82.18 (37.41) | 0.08 |
| ...median [IQR] | 82.00 [62.00, 106.50] | 79.00 [60.00, 102.00] | 0.08 | 84.00 [61.50, 108.00] | 84.00 [62.00, 106.00] | 0.00 | N/A | N/A | #VALUE! | 82.30 (38.73) | 79.67 (37.41) | 0.07 |
| ...Missing; n (%) | 12,558 (65.5%) | 13,017 (67.8%) | -0.05 | 19,628 (94.5%) | 19,828 (95.4%) | -0.04 | N/A | N/A | #VALUE! | 32,186 (80.5%) | 32,845 (82.2%) | -0.04 |
| Lab result number- Total cholesterol (mg/dl) mean (only >=5000 included) | 6,675 | 6,213 | | 1,205 | 1,034 | | N/A | N/A | | 7,880 | 7,247 | |
| ...mean (sd) | 170.81 (45.37) | 167.71 (42.55) | 0.07 | 171.98 (53.53) | 170.54 (48.18) | 0.03 | N/A | N/A | #VALUE! | 170.99 (46.71) | 168.11 (43.40) | 0.06 |
| ...median [IQR] | 164.67 [141.00, 195.00] | 162.00 [139.00, 191.00] | 0.06 | 167.00 [142.00, 199.50] | 166.00 [142.88, 196.00] | 0.02 | N/A | N/A | #VALUE! | 165.03 (46.71) | 162.57 (43.40) | 0.05 |
| ...Missing; n (%) | 12,512 (65.2%) | 12,974 (67.6%) | -0.05 | 19,572 (94.2%) | 19,743 (95.0%) | -0.04 | N/A | N/A | #VALUE! | 32,084 (80.3%) | 32,717 (81.9%) | -0.04 |
| Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) | 6,634 | 6,161 | | 1,193 | 1,016 | | N/A | N/A | | 7,827 | 7,177 | |
| ...mean (sd) | 183.24 (145.11) | 184.97 (135.08) | -0.01 | 188.33 (172.01) | 187.81 (148.81) | 0.00 | N/A | N/A | #VALUE! | 184.02 (149.53) | 185.37 (137.12) | -0.01 |
| ...median [IQR] | 152.00 [109.00, 217.00] | 155.00 [112.00, 218.00] | -0.02 | 149.00 [103.00, 221.25] | 155.00 [109.00, 221.00] | -0.04 | N/A | N/A | #VALUE! | 151.54 (149.53) | 155.00 (137.12) | -0.02 |
| ...Missing; n (%) | 12,553 (65.4%) | 13,026 (67.9%) | -0.05 | 19,584 (94.3%) | 19,761 (95.1%) | -0.04 | N/A | N/A | #VALUE! | 32,137 (80.4%) | 32,787 (82.0%) | -0.04 |
| Lab result number- Hemoglobin mean (only >0 included) | 5,571 | 5,078 | | 891 | 783 | | N/A | N/A | | 6,462 | 5,861 | |
| ...mean (sd) | 13.38 (1.69) | 13.43 (1.61) | -0.03 | 6,166.82 (167,694.97) | 13.30 (2.42) | 0.05 | N/A | N/A | #VALUE! | 861.83 (62249.00) | 13.41 (1.74) | 0.02 |
| ...median [IQR] | 13.40 [12.30, 14.50] | 13.40 [12.40, 14.50] | 0.00 | 13.30 [12.40, 14.45] | 13.45 [12.40, 14.70] | 0.00 | N/A | N/A | #VALUE! | #VALUE! | 13.41 (1.74) | #VALUE! |
| ...Missing; n (%) | 13,616 (71.0%) | 14,109 (73.5%) | -0.06 | 19,886 (95.7%) | 19,994 (96.2%) | -0.03 | N/A | N/A | #VALUE! | 33,502 (83.8%) | 34,103 (85.3%) | -0.04 |
| Lab result number- Serum sodium mean (only >90 and < 190 included) | 7,873 | 7,386 | | 1,270 | 1,096 | | N/A | N/A | | 9,143 | 8,482 | |
| ...mean (sd) | 139.61 (2.73) | 139.62 (2.63) | 0.00 | 139.31 (2.56) | 139.07 (2.53) | 0.09 | N/A | N/A | #VALUE! | 139.57 (2.71) | 139.55 (2.62) | 0.01 |
| ...median [IQR] | 140.00 [138.00, 141.50] | 140.00 [138.00, 141.33] | 0.00 | 139.12 [138.00, 141.00] | 139.00 [137.54, 141.00] | 0.05 | N/A | N/A | #VALUE! | 139.88 (2.71) | 139.87 (2.62) | 0.00 |
| ...Missing; n (%) | 11,314 (59.0%) | 11,801 (61.5%) | -0.05 | 19,507 (93.9%) | 19,681 (94.7%) | -0.03 | N/A | N/A | #VALUE! | 30,821 (77.1%) | 31,482 (78.8%) | -0.04 |
| Lab result number- Albumin mean (only >0 and <=10 included) | 7,378 | 6,868 | | 1,142 | 1,023 | | N/A | N/A | | 8,520 | 7,891 | |
| ...mean (sd) | 4.23 (0.32) | 4.22 (0.31) | 0.03 | 4.11 (0.72) | 4.11 (0.68) | 0.00 | N/A | N/A | #VALUE! | 4.21 (0.40) | 4.21 (0.38) | 0.00 |
| ...median [IQR] | 4.25 [4.00, 4.45] | 4.20 [4.00, 4.40] | 0.16 | 4.20 [4.00, 4.40] | 4.20 [4.00, 4.40] | 0.00 | N/A | N/A | #VALUE! | 4.24 (0.40) | 4.20 (0.38) | 0.10 |
| ...Missing; n (%) | 11,809 (61.5%) | 12,319 (64.2%) | -0.06 | 19,635 (94.5%) | 19,754 (95.1%) | -0.03 | N/A | N/A | #VALUE! | 31,444 (78.7%) | 32,073 (80.3%) | -0.04 |
| Lab result number- Glucose (fasting or random) mean (only 10-1000 included) | 7,859 | 7,362 | | 1,261 | 1,078 | | N/A | N/A | | 9,120 | 8,440 | |
| ...mean (sd) | 168.28 (66.76) | 166.71 (68.39) | 0.02 | 164.30 (62.49) | 168.11 (68.55) | -0.06 | N/A | N/A | #VALUE! | 167.73 (66.19) | 166.89 (68.41) | 0.01 |
| ...median [IQR] | 153.00 [124.00, 196.00] | 151.00 [119.00, 196.00] | 0.03 | 150.00 [121.00, 193.00] | 152.00 [119.00, 197.62] | -0.03 | N/A | N/A | #VALUE! | 152.59 (66.19) | 151.13 (68.41) | 0.02 |
| ...Missing; n (%) | 11,328 (59.0%) | 11,825 (61.6%) | -0.05 | 19,516 (93.9%) | 19,699 (94.8%) | -0.04 | N/A | N/A | #VALUE! | 30,844 (77.2%) | 31,524 (78.9%) | -0.04 |
| Lab result number- Potassium mean (only 1-7 included) | 8,018 | 7,536 | | 1,296 | 1,146 | | N/A | N/A | | 9,314 | 8,682 | |
| ...mean (sd) | 4.45 (0.44) | 4.46 (0.43) | -0.02 | 4.34 (0.45) | 4.36 (0.45) | -0.04 | N/A | N/A | #VALUE! | 4.43 (0.44) | 4.45 (0.43) | -0.05 |
| ...median [IQR] | 4.45 [4.20, 4.70] | 4.45 [4.20, 4.70] | 0.00 | 4.35 [4.00, 4.60] | 4.35 [4.00, 4.60] | 0.00 | N/A | N/A | #VALUE! | 4.44 (0.44) | 4.44 (0.43) | 0.00 |
| ...Missing; n (%) | 11,169 (58.2%) | 11,651 (60.7%) | -0.05 | 19,481 (93.8%) | 19,631 (94.5%) | -0.03 | N/A | N/A | #VALUE! | 30,650 (76.7%) | 31,282 (78.3%) | -0.04 |
| Comorbidity Scores | | | | | | | | | | | | |
| CCI (180 days)- ICD9 and ICD10 | | | | | | | | | | | | |
| ...mean (sd) | 2.81 (1.90) | 2.81 (1.88) | 0.00 | 2.11 (1.53) | 2.10 (1.54) | 0.01 | 2.88 (2.01) | 2.88 (1.99) | 0.00 | 2.67 (1.88) | 2.67 (1.86) | 0.00 |
| ...median [IQR] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 0.00 | 2.00 [1.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 0.00 | 2.00 (1.88) | 2.00 (1.86) | 0.00 |
| Frailty Score: Qualitative Version 365 days as Categories, v1 | | | | | | | | | | | | |
| ...0; n (%) | 9,675 (50.4%) | 9,627 (50.2%) | 0.00 | 6,331 (30.5%) | 6,391 (30.8%) | -0.93 | 14,745 (33.2%) | 14,927 (33.6%) | -0.01 | 30,751 (36.5%) | 30,945 (36.7%) | 0.00 |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|--|---------------------|---------------------|-------|---------------------|---------------------|-------|---------------------|---------------------|-------|----------------|----------------|----------|
| to 2; n (%) | 6,091 (31.7%) | 6,185 (32.2%) | -0.01 | 9,099 (43.8%) | 9,298 (44.8%) | -1.25 | 15,032 (33.9%) | 15,014 (33.8%) | 0.00 | 30,222 (35.8%) | 30,497 (36.2%) | -0.01 |
| ...3 or more; n (%) | 3,421 (17.8%) | 3,375 (17.6%) | 0.01 | 5,347 (25.7%) | 5,088 (24.5%) | 0.03 | 14,604 (32.9%) | 14,440 (32.5%) | 0.01 | 23,372 (27.7%) | 22,903 (27.2%) | 0.01 |
| Frailty Score: Empirical Version 365 days as Categories, | | | | | | | | | | | | |
| ...< 0.12908; n (%) | 3,587 (18.7%) | 3,404 (17.7%) | 0.03 | 3,596 (17.3%) | 3,485 (16.8%) | 0.01 | 4,452 (10.0%) | 4,046 (9.1%) | 0.03 | 11,635 (13.8%) | 10,935 (13.0%) | 0.02 |
| ...0.12908 - 0.1631167; n (%) | 6,091 (31.7%) | 6,047 (31.5%) | 0.00 | 6,834 (32.9%) | 6,788 (32.7%) | 0.00 | 10,566 (23.8%) | 10,686 (24.1%) | -0.01 | 23,491 (27.9%) | 23,521 (27.9%) | 0.00 |
| ...> 0.1631167; n (%) | 9,509 (49.6%) | 9,736 (50.7%) | -0.02 | 10,347 (49.8%) | 10,504 (50.6%) | -0.02 | 29,363 (66.2%) | 29,649 (66.8%) | -0.01 | 49,219 (58.4%) | 49,889 (59.1%) | -0.01 |
| Non-Frailty; n (%) | 11,603 (60.5%) | 11,864 (61.8%) | -0.03 | 11,804 (56.8%) | 11,670 (56.2%) | 0.01 | 1,841 (4.1%) | 1,879 (4.2%) | -0.01 | 25,248 (29.9%) | 25,413 (30.1%) | 0.00 |
| Frailty Score (mean): Qualitative Version 365 days, v1 | | | | | | | | | | | | |
| ...mean (sd) | 1.22 (1.81) | 1.19 (1.72) | 0.02 | 1.69 (1.76) | 1.64 (1.71) | 0.03 | 1.99 (2.19) | 1.96 (2.16) | 0.01 | 1.74 (2.01) | 1.71 (1.96) | 0.02 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 1.00 [0.00, 3.00] | 1.00 [0.00, 2.00] | 0.00 | 1.00 [0.00, 3.00] | 1.00 [0.00, 3.00] | 0.00 | 0.77 (2.01) | 0.77 (1.96) | 0.00 |
| Frailty Score (mean): Empirical Version 365 days, | | | | | | | | | | | | |
| ...mean (sd) | 0.17 (0.06) | 0.17 (0.05) | 0.00 | 0.17 (0.05) | 0.17 (0.05) | 0.00 | 0.20 (0.06) | 0.20 (0.06) | 0.00 | 0.19 (0.06) | 0.19 (0.06) | 0.00 |
| ...median [IQR] | 0.16 [0.14, 0.20] | 0.16 [0.14, 0.20] | 0.00 | 0.16 [0.13, 0.19] | 0.16 [0.13, 0.19] | 0.00 | 0.18 [0.15, 0.23] | 0.18 [0.15, 0.23] | 0.00 | 0.17 (0.06) | 0.17 (0.06) | 0.00 |
| Healthcare Utilization | | | | | | | | | | | | |
| Any hospitalization; n (%) | 1,541 (8.0%) | 1,546 (8.1%) | | 1,803 (8.7%) | 1,753 (8.4%) | | 3,978 (9.0%) | 3,932 (8.9%) | | 7,322 (8.7%) | 7,231 (8.6%) | 0.00 |
| Any hospitalization within prior 30 days; n (%) | 297 (1.5%) | 323 (1.7%) | | 336 (1.6%) | 314 (1.5%) | | 799 (1.8%) | 769 (1.7%) | | 1,432 (1.7%) | 1,406 (1.7%) | 0.00 |
| Any hospitalization during prior 31-180 days; n (%) | 1,301 (6.8%) | 1,288 (6.7%) | | 1,511 (7.3%) | 1,494 (7.2%) | | 3,337 (7.5%) | 3,308 (7.5%) | | 6,149 (7.3%) | 6,090 (7.2%) | 0.00 |
| Endocrinologist Visit; n (%) | 3,589 (18.7%) | 3,976 (20.7%) | | 4,157 (20.0%) | 4,563 (22.0%) | | 9,939 (22.4%) | 10,730 (24.2%) | | 17,685 (21.0%) | 19,269 (22.8%) | -0.04 |
| Endocrinologist Visit (30 days prior); n (%) | 2,456 (12.8%) | 2,552 (13.3%) | | 2,994 (14.4%) | 3,142 (15.1%) | | 6,564 (14.8%) | 6,748 (15.2%) | | 12,014 (14.2%) | 12,442 (14.8%) | -0.02 |
| Endocrinologist Visit (31 to 180 days prior); n (%) | 2,705 (14.1%) | 2,807 (14.6%) | | 3,031 (14.6%) | 3,169 (15.3%) | | 7,860 (17.7%) | 8,000 (18.0%) | | 13,596 (16.1%) | 13,976 (16.6%) | -0.01 |
| Internal medicine/family medicine visits; n (%) | 16,005 (83.4%) | 16,049 (83.6%) | | 17,889 (86.1%) | 17,817 (85.8%) | | 37,186 (83.8%) | 37,213 (83.8%) | | 71,080 (84.3%) | 71,079 (84.3%) | 0.00 |
| Internal medicine/family medicine visits (30 days prior); n (%) | 11,488 (59.9%) | 11,453 (59.7%) | | 12,820 (61.7%) | 12,747 (61.4%) | | 25,129 (56.6%) | 25,010 (56.4%) | | 49,437 (58.6%) | 49,210 (58.3%) | 0.01 |
| Internal medicine/family medicine visits (31 to 180 days prior); n (%) | 14,693 (76.6%) | 14,746 (76.9%) | | 16,264 (78.3%) | 16,214 (78.0%) | | 34,222 (77.1%) | 34,115 (76.9%) | | 65,179 (77.3%) | 65,075 (77.2%) | 0.00 |
| Cardiologist visit; n (%) | 6,554 (34.2%) | 6,623 (34.5%) | | 6,991 (33.6%) | 6,941 (33.4%) | | 16,101 (36.3%) | 16,090 (36.3%) | | 29,646 (35.1%) | 29,654 (35.2%) | 0.00 |
| Number of Cardiologist visits (30 days prior); n (%) | 2,161 (11.3%) | 2,239 (11.7%) | | 2,407 (11.6%) | 2,317 (11.2%) | | 5,233 (11.8%) | 5,130 (11.6%) | | 9,801 (11.6%) | 9,686 (11.5%) | 0.00 |
| Number of Cardiologist visits (31 to 180 days prior); n (%) | 5,709 (29.8%) | 5,679 (29.6%) | | 5,994 (28.8%) | 5,953 (28.7%) | | 14,170 (31.9%) | 14,138 (31.9%) | | 25,873 (30.7%) | 25,770 (30.6%) | 0.00 |
| Electrocardiogram ; n (%) | 6,660 (34.7%) | 6,494 (33.8%) | | 7,436 (35.8%) | 7,460 (35.9%) | | 15,567 (35.1%) | 15,619 (35.2%) | | 29,663 (35.2%) | 29,573 (35.1%) | 0.00 |
| Use of glucose test strips; n (%) | 745 (3.9%) | 797 (4.2%) | | 984 (4.7%) | 992 (4.8%) | | 1,670 (3.9%) | 1,709 (3.9%) | | 3,399 (4.0%) | 3,498 (4.1%) | -0.01 |
| Dialysis; n (%) | 7 (0.0%) | 11 (0.1%) | | 5 (0.0%) | 9 (0.0%) | | 30 (0.1%) | 18 (0.0%) | | 042 (0.0%) | 038 (0.0%) | HD/IV/01 |
| Naive new user v8 ; n (%) | 2,841 (14.8%) | 2,939 (15.3%) | | 2,502 (12.0%) | 2,584 (12.4%) | | 4,759 (10.7%) | 4,824 (10.9%) | | 10,102 (12.0%) | 10,347 (12.3%) | -0.01 |
| N antidiabetic drugs at index date | | | | | | | | | | | | |
| ...mean (sd) | 2.08 (0.83) | 2.07 (0.88) | 0.01 | 2.11 (0.84) | 2.10 (0.90) | 0.01 | 2.12 (0.82) | 2.11 (0.85) | 0.01 | 2.11 (0.83) | 2.10 (0.87) | 0.01 |
| ...median [IQR] | 2.00 [1.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 [2.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 [2.00, 3.00] | 2.00 [1.00, 3.00] | 0.00 | 2.00 (0.83) | 2.00 (0.87) | 0.00 |
| number of different/distinct medication prescriptions | | | | | | | | | | | | |
| ...mean (sd) | 11.67 (5.48) | 11.62 (5.07) | 0.01 | 11.57 (5.27) | 11.49 (4.84) | 0.02 | 11.32 (5.10) | 11.28 (4.68) | 0.01 | 11.46 (5.23) | 11.41 (4.81) | 0.01 |
| ...median [IQR] | 11.00 [8.00, 15.00] | 11.00 [8.00, 14.00] | 0.00 | 11.00 [8.00, 14.00] | 11.00 [8.00, 14.00] | 0.00 | 11.00 [8.00, 14.00] | 11.00 [8.00, 14.00] | 0.00 | 11.00 (5.23) | 11.00 (4.81) | 0.00 |
| Number of Hospitalizations | | | | | | | | | | | | |
| ...mean (sd) | 0.10 (0.36) | 0.10 (0.36) | 0.00 | 0.10 (0.35) | 0.10 (0.35) | 0.00 | 0.11 (0.40) | 0.11 (0.40) | 0.00 | 0.11 (0.38) | 0.11 (0.38) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (0.38) | 0.00 (0.38) | 0.00 |
| Number of hospital days | | | | | | | | | | | | |
| ...mean (sd) | 0.50 (2.40) | 0.49 (2.58) | 0.00 | 0.47 (2.10) | 0.46 (2.30) | 0.00 | 0.64 (2.82) | 0.63 (2.98) | 0.00 | 0.57 (2.57) | 0.56 (2.74) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (2.57) | 0.00 (2.74) | 0.00 |
| Number of Emergency Department (ED) visits | | | | | | | | | | | | |
| ...mean (sd) | 0.42 (1.17) | 0.41 (1.20) | 0.01 | 0.15 (1.58) | 0.16 (1.22) | -0.01 | 0.46 (1.22) | 0.45 (1.22) | 0.01 | 0.37 (1.31) | 0.37 (1.22) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (1.31) | 0.00 (1.22) | 0.00 |
| Number of Office visits | | | | | | | | | | | | |
| ...mean (sd) | 5.85 (4.25) | 5.79 (4.09) | 0.01 | 6.06 (4.48) | 6.03 (4.28) | 0.01 | 6.48 (4.81) | 6.44 (4.59) | 0.01 | 6.23 (4.61) | 6.19 (4.40) | 0.01 |
| ...median [IQR] | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 0.00 | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 0.00 | 5.00 [3.00, 9.00] | 5.00 [3.00, 8.00] | 0.00 | 5.00 (4.61) | 5.00 (4.40) | 0.00 |
| Number of Endocrinologist visits | | | | | | | | | | | | |
| ...mean (sd) | 0.94 (3.12) | 1.08 (3.57) | -0.04 | 1.02 (3.36) | 1.15 (3.67) | -0.04 | 1.37 (4.44) | 1.59 (5.06) | -0.05 | 1.19 (3.92) | 1.37 (4.44) | -0.04 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 (3.92) | 0.00 (4.44) | 0.00 |
| Number of internal medicine/family medicine visits | | | | | | | | | | | | |
| ...mean (sd) | 10.22 (14.26) | 10.41 (14.28) | -0.01 | 7.58 (9.28) | 7.78 (9.68) | -0.02 | 8.74 (11.41) | 8.76 (11.44) | 0.00 | 8.79 (11.66) | 8.89 (11.76) | -0.01 |
| ...median [IQR] | 6.00 [2.00, 13.00] | 6.00 [2.00, 13.00] | 0.00 | 5.00 [2.00, 10.00] | 5.00 [2.00, 10.00] | 0.00 | 5.00 [2.00, 12.00] | 5.00 [2.00, 12.00] | 0.00 | 5.23 (11.66) | 5.23 (11.76) | 0.00 |
| Number of Cardiologist visits | | | | | | | | | | | | |
| ...mean (sd) | 1.73 (4.10) | 1.70 (4.02) | 0.01 | 1.54 (3.79) | 1.53 (3.73) | 0.00 | 1.97 (4.77) | 1.97 (4.91) | 0.00 | 1.81 (4.40) | 1.80 (4.45) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 (4.40) | 0.00 (4.45) | 0.00 |
| Number electrocardiograms received | | | | | | | | | | | | |
| ...mean (sd) | 0.67 (1.37) | 0.67 (1.47) | 0.00 | 0.63 (1.19) | 0.64 (1.21) | -0.01 | 0.70 (1.37) | 0.70 (1.34) | 0.00 | 0.68 (1.33) | 0.68 (1.34) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 (1.33) | 0.00 (1.34) | 0.00 |
| Number of HbA1c tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 1.39 (0.93) | 1.39 (0.92) | 0.00 | 1.14 (0.94) | 1.15 (0.95) | -0.01 | 1.52 (0.87) | 1.52 (0.88) | 0.00 | 1.40 (0.90) | 1.40 (0.91) | 0.00 |
| ...median [IQR] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 0.00 | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 (0.90) | 1.00 (0.91) | 0.00 |
| Number of glucose tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 0.54 (1.37) | 0.57 (1.40) | -0.02 | 0.50 (1.31) | 0.50 (1.20) | 0.00 | 0.50 (1.09) | 0.51 (1.13) | -0.01 | 0.51 (1.21) | 0.52 (1.21) | -0.01 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 (1.21) | 0.00 (1.21) | 0.00 |
| Number of lipid tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 1.09 (0.99) | 1.08 (1.01) | 0.01 | 1.00 (1.33) | 1.00 (1.30) | 0.00 | 1.11 (0.85) | 1.10 (0.88) | 0.01 | 1.08 (1.02) | 1.07 (1.03) | 0.01 |
| ...median [IQR] | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 0.00 | 1.00 [0.00, 1.00] | 1.00 [0.00, 1.00] | 0.00 | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 0.00 | 1.00 (1.02) | 1.00 (1.03) | 0.00 |
| Number of creatinine tests ordered | | | | | | | | | | | | |

Table 1: Liraglutide vs DPP4i

| | | | | | | | | | | | | |
|--|--------------------|--------------------|-------------|-------------------|-------------------|-------------|--------------------|--------------------|-------|----------------|----------------|-------|
| ...mean (sd) | 0.05 (0.30) | 0.06 (0.30) | -0.03 | 0.06 (0.36) | 0.06 (0.34) | 0.00 | 0.09 (0.39) | 0.10 (0.41) | -0.02 | 0.07 (0.36) | 0.08 (0.37) | -0.03 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.36] | 0.00 [0.37] | 0.00 |
| Number of BUN tests ordered | | | | | | | | | | | | |
| ...mean (sd) | 0.03 (0.23) | 0.03 (0.23) | 0.00 | 0.04 (0.27) | 0.04 (0.27) | 0.00 | 0.06 (0.30) | 0.06 (0.32) | 0.00 | 0.05 (0.28) | 0.05 (0.29) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 | 0.00 [0.28] | 0.00 [0.29] | 0.00 |
| Number of tests for microalbuminuria | | | | | | | | | | | | |
| ...mean (sd) | 0.86 (1.24) | 0.86 (1.25) | 0.00 | 0.63 (1.07) | 0.64 (1.07) | -0.01 | 0.56 (0.79) | 0.56 (0.76) | 0.00 | 0.65 (0.98) | 0.65 (0.97) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 | 0.00 [0.98] | 0.00 [0.97] | 0.00 |
| Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level | | | | | | | | | | | | |
| ...mean (sd) | 6.95 (8.39) | 6.93 (8.40) | 0.00 | 2.39 (4.45) | 2.38 (4.64) | 0.00 | 6.22 (8.51) | 6.18 (8.55) | 0.00 | 5.44 (7.68) | 5.41 (7.73) | 0.00 |
| ...median [IQR] | 5.00 [0.00, 10.00] | 5.00 [0.00, 10.00] | 0.00 | 0.00 [0.00, 4.00] | 0.00 [0.00, 4.00] | 0.00 | 4.00 [0.00, 10.00] | 3.00 [0.00, 10.00] | 0.12 | 3.24 (7.68) | 2.72 (7.73) | 0.07 |
| Use of thiazide; n (%) | 2,737 (14.3%) | 2,706 (14.1%) | 0.005729859 | 2,745 (13.2%) | 2,771 (13.3%) | -0.00294956 | 6,857 (15.5%) | 6,900 (15.5%) | 0 | 12,339 (14.6%) | 12,377 (14.7%) | 0.00 |
| Use of beta blockers; n (%) | 8,557 (44.6%) | 8,627 (45.0%) | -0.01 | 9,505 (45.7%) | 9,500 (45.7%) | 0.00 | 21,602 (48.7%) | 21,620 (48.7%) | 0.00 | 39,664 (47.0%) | 39,747 (47.1%) | 0.00 |
| Use of calcium channel blockers; n (%) | 5,718 (29.8%) | 5,741 (29.9%) | 0.00 | 6,185 (29.8%) | 6,269 (30.2%) | -0.01 | 14,181 (32.0%) | 14,361 (32.4%) | -0.01 | 26,084 (30.9%) | 26,371 (31.3%) | -0.01 |

Appendix B: Liraglutide vs 2nd Generation Sulfonylureas

Optum

MarketScan

Medicare

BEFORE PS MATCHING

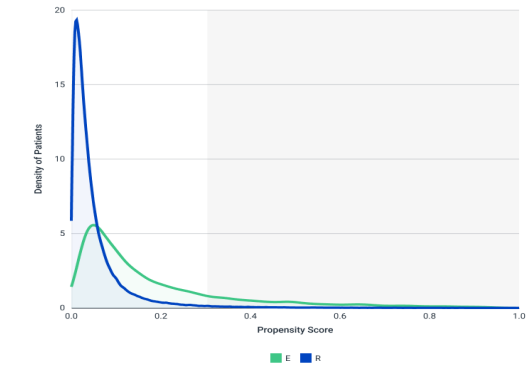


Figure 49: Pre-matching propensity score overlap

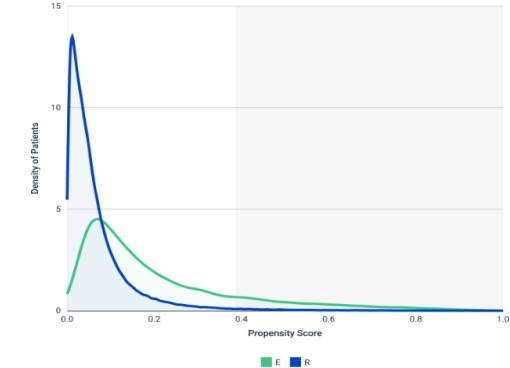


Figure 49: Pre-matching propensity score overlap

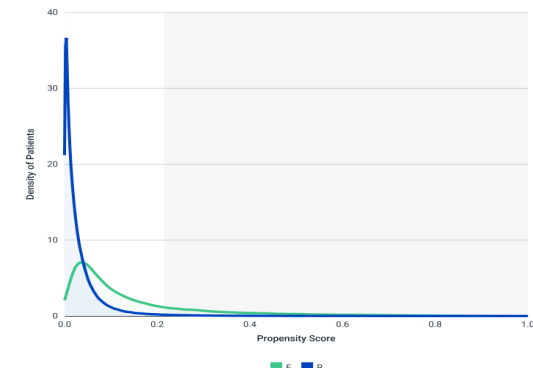


Figure 24: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.815. The post-matching c-statistic was 0.535.

The c-statistics for the propensity score model, pre-matching was 0.811. The post-matching c-statistic was 0.538.

The c-statistics for the propensity score model, pre-matching was 0.835. The post-matching c-statistic was 0.525.

AFTER PS MATCHING

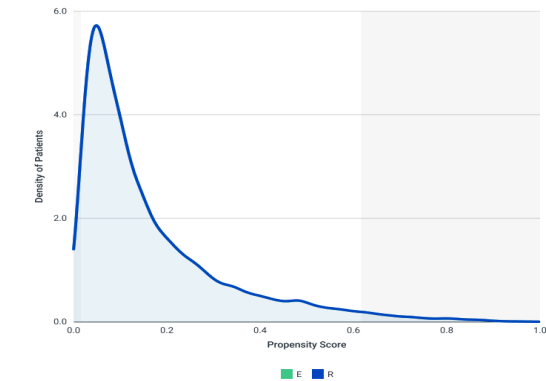


Figure 50: Post-matching propensity score overlap

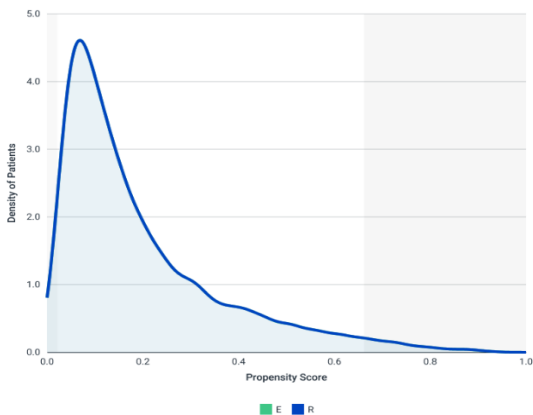


Figure 50: Post-matching propensity score overlap

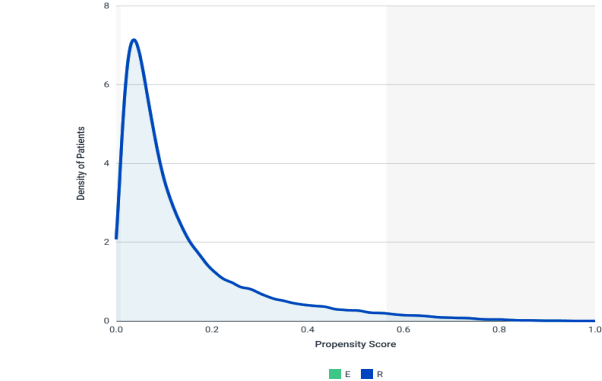


Figure 26: Post-matching propensity score overlap

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| Unmatched | | | | | | | | | |
|---|-------------------------------|-----------------------|-------------------------------|-----------------------|-------------------------------|-----------------------|-------------------------------|-----------------------|-----------|
| Variable | Optum | | MarketScan | | Medicare | | POOLED | | St. Diff. |
| | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | |
| Number of patients | 196,712 | 12,485 | 160,161 | 13,808 | 571,468 | 28,511 | 928,341 | 54,804 | |
| Age | | | | | | | | | |
| ...mean (sd) | 70.45 (7.97) | 65.70 (6.79) | 67.63 (9.31) | 62.85 (6.12) | 74.52 (7.40) | 70.53 (4.98) | 72.47 (7.88) | 67.49 (5.73) | 0.72 |
| ...median [IQR] | 70.00 [65.00, 76.00] | 66.00 [61.00, 70.00] | 65.00 [61.00, 74.00] | 62.00 [60.00, 65.00] | 73.00 [68.00, 79.00] | 3.00 [67.00, 73.00] | 70.98 (7.88) | 66.55 (5.73) | 0.64 |
| Age categories | | | | | | | | | |
| ...18 - 54; n (%) | 4,772 (2.4%) | 740 (5.9%) | 7,998 (5.0%) | 1,177 (8.5%) | 0 (0.0%) | 0 (0.0%) | 12,770 (1.4%) | 1,917 (3.5%) | -0.14 |
| ...55 - 64; n (%) | 38,842 (19.7%) | 4,610 (36.9%) | 70,249 (43.9%) | 8,602 (62.3%) | 9,764 (1.7%) | 694 (2.4%) | 118,855 (12.8%) | 13,906 (25.4%) | -0.32 |
| ...65 - 74; n (%) | 93,525 (47.5%) | 5,912 (47.4%) | 44,191 (27.6%) | 3,328 (24.1%) | 313,203 (54.8%) | 22,386 (78.5%) | 450,919 (48.6%) | 31,626 (57.7%) | -0.18 |
| ...≥ 75; n (%) | 59,573 (30.3%) | 1,223 (9.8%) | 37,723 (23.6%) | 701 (5.1%) | 248,501 (43.5%) | 5,431 (19.0%) | 345,797 (37.2%) | 7,355 (13.4%) | 0.57 |
| Gender | | | | | | | | | |
| ...Males; n (%) | 102,630 (52.2%) | 5,601 (44.9%) | 91,138 (56.9%) | 6,730 (48.7%) | 260,001 (45.5%) | 12,045 (42.2%) | 453,769 (48.9%) | 24,376 (44.5%) | 0.09 |
| ...Females; n (%) | 94,082 (47.8%) | 6,884 (55.1%) | 69,023 (43.1%) | 7,078 (51.3%) | 311,467 (54.5%) | 16,466 (57.8%) | 474,572 (51.1%) | 30,428 (55.5%) | -0.09 |
| Race | | | | | | | | | |
| ...White; n (%) | N/A | N/A | N/A | N/A | 439,116 (76.8%) | 24,090 (84.5%) | 439,116 (76.8%) | 24,090 (84.5%) | -0.20 |
| ...Black; n (%) | N/A | N/A | N/A | N/A | 69,514 (12.2%) | 2,568 (9.0%) | 69,514 (12.2%) | 2,568 (9.0%) | 0.10 |
| ...Asian; n (%) | N/A | N/A | N/A | N/A | 19,245 (3.4%) | 380 (1.3%) | 19,245 (3.4%) | 380 (1.3%) | 0.14 |
| ...Hispanic; n (%) | N/A | N/A | N/A | N/A | 22,497 (3.9%) | 511 (1.8%) | 22,497 (3.9%) | 511 (1.8%) | 0.13 |
| ...North American Native; n (%) | N/A | N/A | N/A | N/A | 3,768 (0.7%) | 122 (0.4%) | 3,768 (0.7%) | 122 (0.4%) | 0.04 |
| ...Other/Unknown; n (%) | N/A | N/A | N/A | N/A | 17,328 (3.0%) | 840 (2.9%) | 17,328 (3.0%) | 840 (2.9%) | 0.01 |
| Region (lumping missing&other category with West) | | | | | | | | | |
| ...Northeast; n (%) | 21,016 (10.7%) | 1,203 (9.6%) | 28,601 (17.9%) | 2,794 (20.2%) | 94,259 (16.5%) | 4,708 (16.5%) | 143,876 (15.5%) | 8,705 (15.9%) | -0.01 |
| ...South; n (%) | 92,464 (47.0%) | 6,770 (54.2%) | 46,370 (29.0%) | 2,793 (20.2%) | 247,501 (43.3%) | 13,088 (45.9%) | 386,335 (41.6%) | 22,651 (41.3%) | 0.01 |
| ...Midwest; n (%) | 38,854 (19.8%) | 2,335 (18.7%) | 61,418 (38.3%) | 6,610 (47.9%) | 138,467 (24.2%) | 6,152 (21.6%) | 238,739 (25.7%) | 15,097 (27.5%) | -0.04 |
| ...West; n (%) | 44,378 (22.6%) | 2,177 (17.4%) | 22,358 (14.0%) | 1,452 (10.5%) | 91,241 (16.0%) | 4,563 (16.0%) | 157,977 (17.0%) | 8,192 (14.9%) | 0.06 |
| ...Unknown+missing; n (%) | N/A | N/A | 1,414 (0.9%) | 159 (1.2%) | N/A | N/A | 1,414 (0.9%) | 159 (1.2%) | -0.03 |
| CV Covariates | | | | | | | | | |
| Ischemic heart disease; n (%) | 55,227 (28.1%) | 3,702 (29.7%) | 52,321 (32.7%) | 4,439 (32.1%) | 187,624 (32.8%) | 8,905 (31.2%) | 295,172 (31.8%) | 17,046 (31.1%) | 0.02 |
| Acute MI; n (%) | 3,262 (1.7%) | 174 (1.4%) | 3,103 (1.9%) | 212 (1.5%) | 10,813 (1.9%) | 338 (1.2%) | 17,178 (1.9%) | 724 (1.3%) | 0.05 |
| ACS/unstable angina; n (%) | 3,647 (1.9%) | 261 (2.1%) | 3,557 (2.2%) | 286 (2.1%) | 11,272 (2.0%) | 482 (1.7%) | 18,476 (2.0%) | 1,029 (1.9%) | 0.01 |
| Old MI; n (%) | 8,091 (4.1%) | 491 (3.9%) | 4,508 (2.8%) | 292 (2.1%) | 26,566 (4.6%) | 1,041 (3.7%) | 39,165 (4.2%) | 1,824 (3.3%) | 0.05 |
| Stable angina; n (%) | 7,795 (4.0%) | 598 (4.8%) | 5,435 (3.4%) | 500 (3.6%) | 21,550 (3.8%) | 1,130 (4.0%) | 34,780 (3.7%) | 2,228 (4.1%) | -0.02 |
| Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%) | 51,300 (26.1%) | 3,479 (27.9%) | 49,443 (30.9%) | 4,229 (30.6%) | 178,665 (31.3%) | 8,493 (29.8%) | 279,408 (30.1%) | 16,201 (29.6%) | 0.01 |
| Other atherosclerosis with ICD10 ; n (%) | 2,423 (1.2%) | 121 (1.0%) | 2,102 (1.3%) | 159 (1.2%) | 11,227 (2.0%) | 473 (1.7%) | 15,752 (1.7%) | 753 (1.4%) | 0.02 |
| Previous cardiac procedure (CABG or PTCA or Stent) ; n (%) | 1,607 (0.8%) | 96 (0.8%) | 1,929 (1.2%) | 140 (1.0%) | 4,469 (0.8%) | 143 (0.5%) | 8,005 (0.9%) | 379 (0.7%) | 0.02 |
| History of CABG or PTCA; n (%) | 12,855 (6.5%) | 921 (7.4%) | 6,551 (4.1%) | 579 (4.2%) | 53,044 (9.3%) | 2,384 (8.4%) | 72,450 (7.8%) | 3,884 (7.1%) | 0.03 |
| Any stroke; n (%) | 16,353 (8.3%) | 905 (7.2%) | 15,031 (9.4%) | 1,024 (7.4%) | 62,700 (11.0%) | 2,451 (8.6%) | 94,084 (10.1%) | 4,380 (8.0%) | 0.07 |
| Ischemic stroke (w and w/o mention of cerebral infarction); n (%) | 16,102 (8.2%) | 900 (7.2%) | 14,822 (9.3%) | 1,006 (7.3%) | 61,905 (10.8%) | 2,428 (8.5%) | 92,829 (10.0%) | 4,334 (7.9%) | 0.07 |
| Hemorrhagic stroke; n (%) | 545 (0.3%) | 16 (0.1%) | 459 (0.3%) | 28 (0.2%) | 2,008 (0.4%) | 45 (0.2%) | 3,012 (0.3%) | 89 (0.2%) | 0.02 |
| TIA; n (%) | 4,010 (2.0%) | 233 (1.9%) | 4,022 (2.5%) | 242 (1.8%) | 14,808 (2.6%) | 516 (1.8%) | 22,840 (2.5%) | 991 (1.8%) | 0.05 |
| Other cerebrovascular disease; n (%) | 4,639 (2.4%) | 230 (1.8%) | 3,239 (2.0%) | 167 (1.2%) | 19,559 (3.4%) | 587 (2.1%) | 27,437 (3.0%) | 984 (1.8%) | 0.08 |
| Late effects of cerebrovascular disease; n (%) | 4,527 (2.3%) | 144 (1.2%) | 2,805 (1.8%) | 95 (0.7%) | 18,669 (3.3%) | 415 (1.5%) | 26,001 (2.8%) | 654 (1.2%) | 0.11 |
| Cerebrovascular procedure; n (%) | 288 (0.1%) | 12 (0.1%) | 311 (0.2%) | 11 (0.1%) | 935 (0.2%) | 26 (0.1%) | 1,534 (0.2%) | 49 (0.1%) | 0.03 |
| Heart failure (CHF); n (%) | 21,366 (10.9%) | 1,275 (10.2%) | 16,040 (10.0%) | 995 (7.2%) | 84,892 (14.9%) | 3,352 (11.8%) | 122,298 (13.2%) | 5,622 (10.3%) | 0.09 |
| Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%) | 18,962 (9.6%) | 1,095 (8.8%) | 14,043 (8.8%) | 1,080 (7.8%) | 73,310 (12.8%) | 2,955 (10.4%) | 106,315 (11.5%) | 5,130 (9.4%) | 0.07 |
| Atrial fibrillation; n (%) | 18,759 (9.5%) | 962 (7.7%) | 13,972 (8.7%) | 789 (5.7%) | 81,612 (14.3%) | 3,081 (10.8%) | 114,343 (12.3%) | 4,832 (8.8%) | 0.11 |
| Other cardiac dysrhythmia; n (%) | 21,281 (10.8%) | 1,309 (10.5%) | 14,014 (8.7%) | 949 (6.9%) | 82,684 (14.5%) | 3,363 (11.8%) | 117,979 (12.7%) | 5,621 (10.3%) | 0.08 |
| Cardiac conduction disorders; n (%) | 6,617 (3.4%) | 355 (2.8%) | 4,460 (2.8%) | 289 (2.1%) | 28,034 (4.9%) | 1,077 (3.8%) | 39,111 (4.2%) | 1,721 (3.1%) | 0.06 |
| Other CVD; n (%) | 26,092 (13.3%) | 1,498 (12.0%) | 20,400 (12.7%) | 1,465 (10.6%) | 99,284 (17.4%) | 4,174 (14.6%) | 145,776 (15.7%) | 7,137 (13.0%) | 0.08 |
| Diabetes-related complications | | | | | | | | | |
| Diabetic retinopathy; n (%) | 11,089 (5.6%) | 956 (7.7%) | 6,538 (4.1%) | 659 (4.8%) | 32,274 (5.6%) | 2,394 (8.4%) | 49,901 (5.4%) | 4,009 (7.3%) | -0.08 |
| Diabetes with other ophthalmic manifestations; n (%) | 1,424 (0.7%) | 91 (0.7%) | 4,704 (2.9%) | 449 (3.3%) | 13,704 (2.4%) | 880 (3.1%) | 19,832 (2.1%) | 1,420 (2.6%) | -0.03 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|---------|
| Retinal detachment, vitreous hemorrhage, vitrectomy; n (%) | 717 (0.4%) | 54 (0.4%) | 464 (0.3%) | 47 (0.3%) | 1,892 (0.3%) | 138 (0.5%) | 3,073 (0.3%) | 239 (0.4%) | -0.02 |
| Retinal laser coagulation therapy; n (%) | 944 (0.5%) | 75 (0.6%) | 860 (0.5%) | 92 (0.7%) | 2,550 (0.4%) | 201 (0.7%) | 4,354 (0.5%) | 368 (0.7%) | -0.03 |
| Occurrence of Diabetic Neuropathy ; n (%) | 34,538 (17.6%) | 2,995 (24.0%) | 17,014 (10.6%) | 1,961 (14.2%) | 95,992 (16.8%) | 6,700 (23.5%) | 147,478 (15.9%) | 11,656 (21.3%) | -0.14 |
| Occurrence of diabetic nephropathy with ICD10 ; n (%) | 31,872 (16.2%) | 2,161 (17.3%) | 11,026 (6.9%) | 1,042 (7.5%) | 54,295 (9.5%) | 3,539 (12.4%) | 97,193 (10.5%) | 6,742 (12.3%) | -0.06 |
| Hypoglycemia ; n (%) | 5,003 (2.5%) | 275 (2.2%) | 5,026 (3.1%) | 413 (3.0%) | 16,139 (2.8%) | 853 (3.0%) | 26,168 (2.8%) | 1,541 (2.8%) | 0.00 |
| Hyperglycemia; n (%) | 8,676 (4.4%) | 579 (4.6%) | 5,054 (3.2%) | 429 (3.1%) | 29,706 (5.2%) | 1,240 (4.3%) | 43,436 (4.7%) | 2,248 (4.1%) | 0.03 |
| Disorders of fluid electrolyte and acid-base balance; n (%) | 17,943 (9.1%) | 827 (6.6%) | 11,019 (6.9%) | 607 (4.4%) | 69,422 (12.1%) | 2,164 (7.6%) | 98,384 (10.6%) | 3,598 (6.6%) | 0.14 |
| Diabetic ketoacidosis; n (%) | 210 (0.1%) | 14 (0.1%) | 153 (0.1%) | 17 (0.1%) | 731 (0.1%) | 33 (0.1%) | 1,094 (0.1%) | 64 (0.1%) | 0.00 |
| Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%) | 1,026 (0.5%) | 70 (0.6%) | 579 (0.4%) | 44 (0.3%) | 2,876 (0.5%) | 128 (0.4%) | 4,481 (0.5%) | 242 (0.4%) | 0.01 |
| Diabetes with peripheral circulatory disorders with ICD-10 ; n (%) | 15,191 (7.7%) | 987 (7.9%) | 6,670 (4.2%) | 540 (3.9%) | 42,778 (7.5%) | 2,040 (7.2%) | 64,639 (7.0%) | 3,567 (6.5%) | 0.02 |
| Diabetic Foot; n (%) | 4,860 (2.5%) | 320 (2.6%) | 3,959 (2.5%) | 304 (2.2%) | 18,615 (3.3%) | 940 (3.3%) | 27,434 (3.0%) | 1,564 (2.9%) | 0.01 |
| Gangrene ; n (%) | 669 (0.3%) | 34 (0.3%) | 552 (0.3%) | 20 (0.1%) | 2,088 (0.4%) | 60 (0.2%) | 3,309 (0.4%) | 114 (0.2%) | 0.04 |
| Lower extremity amputation; n (%) | 1,382 (0.7%) | 109 (0.9%) | 710 (0.4%) | 41 (0.3%) | 4,515 (0.8%) | 165 (0.6%) | 6,607 (0.7%) | 315 (0.6%) | 0.01 |
| Osteomyelitis; n (%) | 1,371 (0.7%) | 88 (0.7%) | 1,120 (0.7%) | 66 (0.5%) | 4,379 (0.8%) | 168 (0.6%) | 6,870 (0.7%) | 322 (0.6%) | 0.01 |
| Skin infections ; n (%) | 11,149 (5.7%) | 742 (5.9%) | 9,819 (6.1%) | 811 (5.9%) | 43,277 (7.6%) | 2,258 (7.9%) | 64,245 (6.9%) | 3,811 (7.0%) | 0.00 |
| Erectile dysfunction; n (%) | 4,789 (2.4%) | 360 (2.9%) | 3,269 (2.0%) | 318 (2.3%) | 10,887 (1.9%) | 833 (2.9%) | 18,945 (2.0%) | 1,511 (2.8%) | -0.05 |
| Diabetes with unspecified complication; n (%) | 9,112 (4.6%) | 827 (6.6%) | 5,419 (3.4%) | 659 (4.8%) | 25,116 (4.4%) | 1,673 (5.9%) | 39,647 (4.3%) | 3,159 (5.8%) | -0.07 |
| Diabetes mellitus without mention of complications; n (%) | 174,528 (88.7%) | 10,824 (86.7%) | 150,098 (93.7%) | 12,905 (93.5%) | 539,347 (94.4%) | 26,472 (92.8%) | 863,973 (93.1%) | 50,201 (91.6%) | 0.06 |
| Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%) | 185,514 (94.3%) | 11,887 (95.2%) | 139,282 (87.0%) | 12,287 (89.0%) | 550,194 (96.3%) | 27,630 (96.9%) | 874,990 (94.3%) | 51,804 (94.5%) | -0.01 |
| Hyperlipidemia ; n (%) | 144,099 (73.3%) | 9,851 (78.9%) | 99,840 (62.3%) | 9,823 (71.1%) | 435,198 (76.2%) | 23,633 (82.9%) | 679,137 (73.2%) | 43,307 (79.0%) | -0.14 |
| Edema; n (%) | 14,841 (7.5%) | 1,088 (8.7%) | 9,129 (5.7%) | 846 (6.1%) | 62,616 (11.0%) | 3,218 (11.3%) | 86,586 (9.3%) | 5,152 (9.4%) | 0.00 |
| Renal Dysfunction (non-diabetic) ; n (%) | 50,792 (25.8%) | 2,889 (23.1%) | 27,130 (16.9%) | 1,892 (13.7%) | 141,930 (24.8%) | 6,290 (22.1%) | 219,852 (23.7%) | 11,071 (20.2%) | 0.08 |
| Occurrence of acute renal disease ; n (%) | 9,401 (4.8%) | 369 (3.0%) | 6,016 (3.8%) | 216 (1.6%) | 35,473 (6.2%) | 909 (3.2%) | 50,890 (5.5%) | 1,494 (2.7%) | 0.14 |
| Occurrence of chronic renal insufficiency; n (%) | 42,651 (21.7%) | 2,481 (19.9%) | 19,946 (12.5%) | 1,449 (10.5%) | 116,950 (20.5%) | 5,396 (18.9%) | 179,547 (19.3%) | 9,326 (17.0%) | 0.06 |
| Chronic kidney disease ; n (%) | 41,223 (21.0%) | 2,405 (19.3%) | 19,353 (12.1%) | 1,392 (10.1%) | 111,247 (19.5%) | 5,116 (17.9%) | 171,823 (18.5%) | 8,913 (16.3%) | 0.06 |
| CKD Stage 3-4; n (%) | 29,293 (14.9%) | 1,735 (13.9%) | 13,900 (8.7%) | 1,030 (7.5%) | 76,878 (13.5%) | 3,680 (12.9%) | 120,071 (12.9%) | 6,445 (11.8%) | 0.03 |
| Occurrence of hypertensive nephropathy; n (%) | 18,774 (9.5%) | 1,084 (8.7%) | 8,031 (5.0%) | 535 (3.9%) | 56,974 (10.0%) | 2,269 (8.0%) | 83,779 (9.0%) | 3,888 (7.1%) | 0.07 |
| Occurrence of miscellaneous renal insufficiency ; n (%) | 12,325 (6.3%) | 641 (5.1%) | 7,652 (4.8%) | 513 (3.7%) | 45,632 (8.0%) | 1,823 (6.4%) | 65,609 (7.1%) | 2,977 (5.4%) | 0.07 |
| Glaucoma or cataracts ; n (%) | 41,679 (21.2%) | 2,571 (20.6%) | 28,496 (17.8%) | 2,350 (17.0%) | 144,998 (25.4%) | 8,094 (28.4%) | 215,173 (23.2%) | 13,015 (23.7%) | -0.01 |
| Cellulitis or abscess of toe; n (%) | 2,852 (1.4%) | 189 (1.5%) | 1,698 (1.1%) | 126 (0.9%) | 9,051 (1.6%) | 446 (1.6%) | 13,601 (1.5%) | 761 (1.4%) | 0.01 |
| Foot ulcer; n (%) | 4,802 (2.4%) | 302 (2.4%) | 4,015 (2.5%) | 304 (2.2%) | 18,697 (3.3%) | 921 (3.2%) | 27,514 (3.0%) | 1,527 (2.8%) | 0.01 |
| Bladder stones; n (%) | 269 (0.1%) | 8 (0.1%) | 223 (0.1%) | 14 (0.1%) | 1,039 (0.2%) | 41 (0.1%) | 1,531 (0.2%) | 63 (0.1%) | 0.03 |
| Kidney stones; n (%) | 4,100 (2.1%) | 318 (2.5%) | 3,487 (2.2%) | 341 (2.5%) | 14,180 (2.5%) | 805 (2.8%) | 21,767 (2.3%) | 1,464 (2.7%) | -0.03 |
| Urinary tract infections (UTIs); n (%) | 19,351 (9.8%) | 1,136 (9.1%) | 11,757 (7.3%) | 940 (6.8%) | 84,914 (14.9%) | 3,659 (12.8%) | 116,022 (12.5%) | 5,735 (10.5%) | 0.06 |
| Dipstick urinalysis; n (%) | 68,120 (34.6%) | 4,493 (36.0%) | 46,700 (29.2%) | 4,559 (33.0%) | 223,752 (39.2%) | 11,639 (40.8%) | 338,572 (36.5%) | 20,691 (37.8%) | -0.03 |
| Non-dipstick urinalysis; n (%) | 76,422 (38.8%) | 5,479 (43.9%) | 42,377 (26.5%) | 4,897 (35.5%) | 205,498 (36.0%) | 13,140 (46.1%) | 324,297 (34.9%) | 23,516 (42.9%) | -0.16 |
| Urine function test; n (%) | 4,806 (2.4%) | 280 (2.2%) | 4,075 (2.5%) | 345 (2.5%) | 17,903 (3.1%) | 986 (3.5%) | 26,784 (2.9%) | 1,611 (2.9%) | 0.00 |
| Cytology; n (%) | 1,477 (0.8%) | 85 (0.7%) | 1,544 (1.0%) | 115 (0.8%) | 5,802 (1.0%) | 288 (1.0%) | 8,823 (1.0%) | 488 (0.9%) | 0.01 |
| Cystos; n (%) | 2,368 (1.2%) | 147 (1.2%) | 2,245 (1.4%) | 176 (1.3%) | 8,292 (1.5%) | 418 (1.5%) | 12,905 (1.4%) | 741 (1.4%) | 0.00 |
| Other Covariates | | | | | | | | | |
| Liver disease; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | #VALUE! | 000 (0.0%) | #VALUE! |
| Osteoarthritis; n (%) | 33,853 (17.2%) | 2,542 (20.4%) | 21,855 (13.6%) | 2,219 (16.1%) | 136,870 (24.0%) | 7,450 (26.1%) | 192,578 (20.7%) | 12,211 (22.3%) | -0.04 |
| Other arthritis, arthropathies and musculoskeletal pain; n (%) | 71,081 (36.1%) | 5,138 (41.2%) | 53,785 (33.6%) | 5,188 (37.6%) | 259,992 (45.5%) | 13,940 (48.9%) | 384,858 (41.5%) | 24,266 (44.3%) | -0.06 |
| Dorsopathies; n (%) | 41,440 (21.1%) | 3,364 (26.9%) | 30,075 (18.8%) | 3,095 (22.4%) | 150,059 (26.3%) | 8,971 (31.5%) | 221,574 (23.9%) | 15,430 (28.2%) | -0.10 |
| Fractures; n (%) | 6,554 (3.3%) | 371 (3.0%) | 5,196 (3.2%) | 351 (2.5%) | 26,453 (4.6%) | 1,070 (3.8%) | 38,203 (4.1%) | 1,792 (3.3%) | 0.04 |
| Falls ; n (%) | 7,893 (4.0%) | 372 (3.0%) | 2,427 (1.5%) | 138 (1.0%) | 31,012 (5.4%) | 971 (3.4%) | 41,332 (4.5%) | 1,481 (2.7%) | 0.10 |
| Osteoporosis; n (%) | 10,537 (5.4%) | 556 (4.5%) | 5,586 (3.5%) | 427 (3.1%) | 44,053 (7.7%) | 2,028 (7.1%) | 60,176 (6.5%) | 3,011 (5.5%) | 0.04 |
| Hyperthyroidism; n (%) | 1,325 (0.7%) | 102 (0.8%) | 756 (0.5%) | 72 (0.5%) | 5,224 (0.9%) | 285 (1.0%) | 7,305 (0.8%) | 459 (0.8%) | 0.00 |
| Hypothyroidism ; n (%) | 29,473 (15.0%) | 2,544 (20.4%) | 16,299 (10.2%) | 2,095 (15.2%) | 84,955 (14.9%) | 5,114 (17.9%) | 130,727 (14.1%) | 9,753 (17.8%) | -0.10 |
| Other disorders of thyroid gland ; n (%) | 5,691 (2.9%) | 690 (5.5%) | 3,833 (2.4%) | 717 (5.2%) | 19,904 (3.5%) | 1,782 (6.3%) | 29,428 (3.2%) | 3,189 (5.8%) | -0.13 |
| Depression; n (%) | 15,620 (7.9%) | 1,336 (10.7%) | 10,206 (6.4%) | 1,173 (8.5%) | 65,406 (11.4%) | 3,664 (12.9%) | 91,232 (9.8%) | 6,173 (11.3%) | -0.05 |
| Anxiety; n (%) | 12,813 (6.5%) | 1,186 (9.5%) | 6,953 (4.3%) | 770 (5.6%) | 50,865 (8.9%) | 2,569 (9.0%) | 70,631 (7.6%) | 4,525 (8.3%) | -0.03 |
| Sleep Disorder; n (%) | 12,444 (6.3%) | 1,304 (10.4%) | 13,885 (8.7%) | 2,243 (16.2%) | 49,765 (8.7%) | 3,988 (14.0%) | 76,094 (8.2%) | 7,535 (13.7%) | -0.18 |
| Dementia; n (%) | 10,450 (5.3%) | 258 (2.1%) | 6,100 (3.8%) | 146 (1.1%) | 54,395 (9.5%) | 1,006 (3.5%) | 70,945 (7.6%) | 1,410 (2.6%) | 0.23 |
| Delirium; n (%) | 3,084 (1.6%) | 93 (0.7%) | 2,269 (1.4%) | 69 (0.5%) | 16,516 (2.9%) | 351 (1.2%) | 21,869 (2.4%) | 513 (0.9%) | 0.12 |
| Psychosis; n (%) | 2,498 (1.3%) | 81 (0.6%) | 1,727 (1.1%) | 57 (0.4%) | 15,982 (2.8%) | 256 (0.9%) | 20,207 (2.2%) | 394 (0.7%) | 0.13 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|-----------------|---------------|-----------------|---------------|-----------------|----------------|-----------------|----------------|---------|
| Obesity; n (%) | 31,831 (16.2%) | 4,320 (34.6%) | 16,930 (10.6%) | 3,086 (22.3%) | 77,359 (13.5%) | 7,939 (27.8%) | 126,120 (13.6%) | 15,345 (28.0%) | -0.36 |
| Overweight; n (%) | 9,079 (4.6%) | 534 (4.3%) | 2,442 (1.5%) | 267 (1.9%) | 17,903 (3.1%) | 820 (2.9%) | 29,424 (3.2%) | 1,621 (3.0%) | 0.01 |
| Smoking; n (%) | 20,336 (10.3%) | 1,403 (11.2%) | 8,760 (5.5%) | 632 (4.6%) | 77,008 (13.5%) | 3,563 (12.5%) | 106,104 (11.4%) | 5,598 (10.2%) | 0.04 |
| Alcohol abuse or dependence; n (%) | 1,443 (0.7%) | 47 (0.4%) | 840 (0.5%) | 38 (0.3%) | 4,133 (0.7%) | 97 (0.3%) | 6,416 (0.7%) | 182 (0.3%) | 0.06 |
| Drug abuse or dependence; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | #VALUE! | 00 (0.0%) | #VALUE! |
| COPD; n (%) | 17,677 (9.0%) | 1,036 (8.3%) | 10,715 (6.7%) | 671 (4.9%) | 76,066 (13.3%) | 3,280 (11.5%) | 104,458 (11.3%) | 4,987 (9.1%) | 0.07 |
| Asthma; n (%) | 9,916 (5.0%) | 930 (7.4%) | 6,975 (4.4%) | 821 (5.9%) | 37,105 (6.5%) | 2,443 (8.6%) | 53,996 (5.8%) | 4,194 (7.7%) | -0.08 |
| Obstructive sleep apnea; n (%) | 14,202 (7.2%) | 2,283 (18.3%) | 12,619 (7.9%) | 2,406 (17.4%) | 38,734 (6.8%) | 4,306 (15.1%) | 65,555 (7.1%) | 8,995 (16.4%) | -0.29 |
| Pneumonia; n (%) | 5,880 (3.0%) | 256 (2.1%) | 4,981 (3.1%) | 241 (1.7%) | 28,237 (4.9%) | 795 (2.8%) | 39,098 (4.2%) | 1,292 (2.4%) | 0.10 |
| Imaging; n (%) | 349 (0.2%) | 15 (0.1%) | 247 (0.2%) | 10 (0.1%) | 1,541 (0.3%) | 34 (0.1%) | 2,137 (0.2%) | 59 (0.1%) | 0.03 |
| Diabetes Medications | | | | | | | | | |
| DM Medications - AGIs; n (%) | 658 (0.3%) | 40 (0.3%) | 522 (0.3%) | 48 (0.3%) | 2,010 (0.4%) | 121 (0.4%) | 3,190 (0.3%) | 209 (0.4%) | -0.02 |
| DM Medications - Glitazones; n (%) | 16,520 (8.4%) | 1,216 (9.7%) | 17,287 (10.8%) | 1,827 (13.2%) | 37,921 (6.6%) | 2,572 (9.0%) | 71,728 (7.7%) | 5,615 (10.2%) | -0.09 |
| DM Medications - Insulin; n (%) | 11,363 (5.8%) | 2,682 (21.5%) | 9,783 (6.1%) | 2,740 (19.8%) | 40,963 (7.2%) | 7,037 (24.7%) | 62,109 (6.7%) | 12,459 (22.7%) | -0.46 |
| DM Medications - Meglitinides; n (%) | 1,281 (0.7%) | 146 (1.2%) | 1,525 (1.0%) | 311 (2.3%) | 5,854 (1.0%) | 590 (2.1%) | 8,660 (0.9%) | 1,047 (1.9%) | -0.09 |
| DM Medications - Metformin; n (%) | 125,476 (63.8%) | 7,325 (58.7%) | 100,419 (62.7%) | 8,570 (62.1%) | 355,150 (62.1%) | 17,242 (60.5%) | 581,045 (62.6%) | 33,137 (60.5%) | 0.04 |
| Concomitant initiation or current use of SGLT2i; n (%) | 2,699 (1.4%) | 717 (5.7%) | 1,961 (1.2%) | 731 (5.3%) | 4,774 (0.8%) | 1,220 (4.3%) | 9,434 (1.0%) | 2,668 (4.9%) | -0.23 |
| Concomitant initiation or current use of AGIs; n (%) | 472 (0.2%) | 22 (0.2%) | 391 (0.2%) | 29 (0.2%) | 1,434 (0.3%) | 83 (0.3%) | 2,297 (0.2%) | 134 (0.2%) | 0.00 |
| Concomitant initiation or current use of Glitazones; n (%) | 12,440 (6.3%) | 873 (7.0%) | 12,991 (8.1%) | 1,304 (9.4%) | 28,770 (5.0%) | 1,961 (6.9%) | 54,201 (5.8%) | 4,138 (7.6%) | -0.07 |
| Concomitant initiation or current use of DPP4i ; n (%) | 4,204 (2.1%) | 109 (0.9%) | 4,943 (3.1%) | 124 (0.9%) | 13,128 (2.3%) | 225 (0.8%) | 22,275 (2.4%) | #VALUE! | #VALUE! |
| Concomitant initiation or current use of Insulin; n (%) | 6,048 (3.1%) | 1,683 (13.5%) | 5,661 (3.5%) | 1,712 (12.4%) | 22,161 (3.9%) | 4,433 (15.5%) | 33,870 (3.6%) | 7,828 (14.3%) | -0.38 |
| Concomitant initiation or current use of Meglitinides; n (%) | 781 (0.4%) | 86 (0.7%) | 931 (0.6%) | 215 (1.6%) | 3,651 (0.6%) | 402 (1.4%) | 5,363 (0.6%) | 703 (1.3%) | -0.07 |
| Concomitant initiation or current use of Metformin; n (%) | 105,292 (53.5%) | 5,852 (46.9%) | 83,840 (52.3%) | 6,810 (49.3%) | 296,366 (51.9%) | 13,865 (48.6%) | 485,498 (52.3%) | 26,527 (48.4%) | 0.08 |
| Past use of SGLT2i ; n (%) | 1,362 (0.7%) | 294 (2.4%) | 795 (0.5%) | 249 (1.8%) | 2,664 (0.5%) | 540 (1.9%) | 4,821 (0.5%) | 1,083 (2.0%) | -0.14 |
| Past use of AGIs ; n (%) | 186 (0.1%) | 18 (0.1%) | 131 (0.1%) | 19 (0.1%) | 576 (0.1%) | 38 (0.1%) | 893 (0.1%) | 75 (0.1%) | 0.00 |
| Past use of Glitazones ; n (%) | 4,080 (2.1%) | 343 (2.7%) | 4,296 (2.7%) | 523 (3.8%) | 9,151 (1.6%) | 611 (2.1%) | 17,527 (1.9%) | 1,477 (2.7%) | -0.05 |
| Past use of DPP4i ; n (%) | 4,798 (2.4%) | 474 (3.8%) | 4,852 (3.0%) | 747 (5.4%) | 17,036 (3.0%) | 1,321 (4.6%) | 26,686 (2.9%) | 2,542 (4.6%) | -0.09 |
| Past use of Insulin ; n (%) | 5,316 (2.7%) | 999 (8.0%) | 4,122 (2.6%) | 1,028 (7.4%) | 18,807 (3.3%) | 2,604 (9.1%) | 28,245 (3.0%) | 4,631 (8.5%) | -0.24 |
| Past use of Meglitinides ; n (%) | 500 (0.3%) | 60 (0.5%) | 594 (0.4%) | 96 (0.7%) | 2,203 (0.4%) | 188 (0.7%) | 3,297 (0.4%) | 344 (0.6%) | -0.03 |
| Past use of metformin (final) ; n (%) | 20,184 (10.3%) | 1,473 (11.8%) | 16,579 (10.4%) | 1,760 (12.7%) | 58,784 (10.3%) | 3,377 (11.8%) | 95,547 (10.3%) | 6,610 (12.1%) | -0.06 |
| Other Medications | | | | | | | | | |
| Use of ACE inhibitors; n (%) | 95,481 (48.5%) | 5,189 (41.6%) | 75,829 (47.3%) | 5,623 (40.7%) | 267,223 (46.8%) | 11,669 (40.9%) | 438,533 (47.2%) | 22,481 (41.0%) | 0.13 |
| Use of ARBs; n (%) | 50,472 (25.7%) | 4,265 (34.2%) | 43,683 (27.3%) | 5,149 (37.3%) | 155,237 (27.2%) | 10,277 (36.0%) | 249,392 (26.9%) | 19,691 (35.9%) | -0.19 |
| Use of Loop Diuretics ; n (%) | 29,814 (15.2%) | 2,153 (17.2%) | 25,579 (16.0%) | 2,138 (15.5%) | 122,938 (21.5%) | 6,242 (21.9%) | 178,331 (19.2%) | 10,533 (19.2%) | 0.00 |
| Use of other diuretics; n (%) | 6,145 (3.1%) | 543 (4.3%) | 5,612 (3.5%) | 609 (4.4%) | 22,856 (4.0%) | 1,451 (5.1%) | 34,613 (3.7%) | 2,603 (4.7%) | -0.05 |
| Use of nitrates-United; n (%) | 13,013 (6.6%) | 889 (7.1%) | 13,267 (8.3%) | 986 (7.1%) | 50,608 (8.9%) | 2,246 (7.9%) | 76,888 (8.3%) | 4,121 (7.5%) | 0.03 |
| Use of other hypertension drugs; n (%) | 17,387 (8.8%) | 893 (7.2%) | 13,879 (8.7%) | 917 (6.6%) | 55,688 (9.7%) | 2,257 (7.9%) | 86,954 (9.4%) | 4,067 (7.4%) | 0.07 |
| Use of digoxin; n (%) | 4,907 (2.5%) | 177 (1.4%) | 4,877 (3.0%) | 221 (1.6%) | 22,362 (3.9%) | 602 (2.1%) | 32,146 (3.5%) | 1,000 (1.8%) | 0.11 |
| Use of Anti-arrhythmics; n (%) | 3,586 (1.8%) | 208 (1.7%) | 3,575 (2.2%) | 229 (1.7%) | 15,299 (2.7%) | 638 (2.2%) | 22,460 (2.4%) | 1,075 (2.0%) | 0.03 |
| Use of COPD/asthma meds; n (%) | 24,498 (12.5%) | 2,132 (17.1%) | 21,896 (13.7%) | 2,435 (17.6%) | 92,859 (16.2%) | 5,747 (20.2%) | 139,253 (15.0%) | 10,314 (18.8%) | -0.10 |
| Use of statins; n (%) | 129,470 (65.8%) | 8,672 (69.5%) | 104,551 (65.3%) | 9,624 (69.7%) | 379,136 (66.3%) | 20,297 (71.2%) | 613,157 (66.0%) | 38,593 (70.4%) | -0.09 |
| Use of other lipid-lowering drugs; n (%) | 20,454 (10.4%) | 1,705 (13.7%) | 22,311 (13.9%) | 2,476 (17.9%) | 62,387 (10.9%) | 4,234 (14.9%) | 105,152 (11.3%) | 8,415 (15.4%) | -0.12 |
| Use of antiplatelet agents; n (%) | 26,712 (13.6%) | 1,885 (15.1%) | 29,039 (18.1%) | 2,574 (18.6%) | 88,937 (15.6%) | 4,508 (15.8%) | 144,688 (15.6%) | 8,967 (16.4%) | -0.02 |
| Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%) | 15,431 (7.8%) | 898 (7.2%) | 13,337 (8.3%) | 865 (6.3%) | 64,168 (11.2%) | 2,746 (9.6%) | 92,936 (10.0%) | 4,509 (8.2%) | 0.06 |
| Use of heparin and other low-molecular weight heparins; n (%) | 997 (0.5%) | 70 (0.6%) | 42 (0.0%) | 0 (0.0%) | 3,443 (0.6%) | 141 (0.5%) | 4,482 (0.5%) | 211 (0.4%) | 0.01 |
| Use of NSAIDs; n (%) | 27,926 (14.2%) | 2,195 (17.6%) | 22,554 (14.1%) | 2,437 (17.6%) | 88,637 (15.5%) | 5,192 (18.2%) | 139,117 (15.0%) | 9,824 (17.9%) | -0.08 |
| Use of oral corticosteroids; n (%) | 29,383 (14.9%) | 2,095 (16.8%) | 24,298 (15.2%) | 2,189 (15.9%) | 105,691 (18.5%) | 5,314 (18.6%) | 159,372 (17.2%) | 9,598 (17.5%) | -0.01 |
| Use of bisphosphonate (United); n (%) | 5,538 (2.8%) | 246 (2.0%) | 3,396 (2.1%) | 213 (1.5%) | 18,770 (3.3%) | 730 (2.6%) | 27,704 (3.0%) | 1,189 (2.2%) | 0.05 |
| Use of opioids; n (%) | 46,368 (23.6%) | 3,558 (28.5%) | 41,697 (26.0%) | 3,960 (28.7%) | 152,202 (26.6%) | 8,558 (30.0%) | 240,267 (25.9%) | 16,076 (29.3%) | -0.08 |
| Use of antidepressants; n (%) | 40,204 (20.4%) | 3,993 (32.0%) | 32,509 (20.3%) | 4,226 (30.6%) | 141,130 (24.7%) | 9,732 (34.1%) | 213,843 (23.0%) | 17,951 (32.8%) | -0.22 |
| Use of antipsychotics; n (%) | 4,150 (2.1%) | 303 (2.4%) | 3,031 (1.9%) | 263 (1.9%) | 20,868 (3.7%) | 741 (2.6%) | 28,049 (3.0%) | 1,307 (2.4%) | 0.04 |
| Use of anticonvulsants; n (%) | 27,511 (14.0%) | 2,594 (20.8%) | 18,209 (11.4%) | 2,061 (14.9%) | 93,566 (16.4%) | 5,868 (20.6%) | 139,286 (15.0%) | 10,523 (19.2%) | -0.11 |
| Use of lithium; n (%) | 205 (0.1%) | 12 (0.1%) | 203 (0.1%) | 16 (0.1%) | 735 (0.1%) | 38 (0.1%) | 1,143 (0.1%) | 066 (0.1%) | 0.00 |
| Use of Benzos; n (%) | 15,195 (7.7%) | 1,491 (11.9%) | 16,820 (10.5%) | 1,814 (13.1%) | 56,618 (9.9%) | 3,401 (11.9%) | 88,633 (9.5%) | 6,706 (12.2%) | -0.09 |
| Use of anxiolytics/hypnotics; n (%) | 9,918 (5.0%) | 963 (7.7%) | 9,756 (6.1%) | 1,225 (8.9%) | 34,826 (6.1%) | 2,308 (8.1%) | 54,500 (5.9%) | 4,496 (8.2%) | -0.09 |
| Use of dementia meds; n (%) | 5,629 (2.9%) | 120 (1.0%) | 3,983 (2.5%) | 99 (0.7%) | 30,389 (5.3%) | 615 (2.2%) | 40,001 (4.3%) | 834 (1.5%) | 0.17 |
| Use of antiparkinsonian meds; n (%) | 4,469 (2.3%) | 437 (3.5%) | 3,486 (2.2%) | 441 (3.2%) | 19,549 (3.4%) | 1,259 (4.4%) | 27,504 (3.0%) | 2,137 (3.9%) | -0.05 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|----------------|--------------|-----------------|------------------|---------|
| Any use of pramlintide; n (%) | 3 (0.0%) | 5 (0.0%) | 8 (0.0%) | 25 (0.2%) | 4 (0.0%) | 17 (0.1%) | 015 (0.0%) | 047 (0.1%) | -0.04 |
| Any use of 1st generation sulfonylureas; n (%) | 75 (0.0%) | 0 (0.0%) | 164 (0.1%) | 1 (0.0%) | 373 (0.1%) | 3 (0.0%) | 612 (0.1%) | 004 (0.0%) | 0.00 |
| Entresto (sacubitril/valsartan); n (%) | 199 (0.1%) | 38 (0.3%) | 56 (0.0%) | 9 (0.1%) | 291 (0.1%) | 26 (0.1%) | 546 (0.1%) | 073 (0.1%) | 0.00 |
| Initiation as monotherapy ; n (%) | 34,741 (17.7%) | 1,801 (14.4%) | 25,845 (16.1%) | 1,561 (11.3%) | 86,804 (15.2%) | 2,776 (9.7%) | 147,390 (15.9%) | 6,138 (11.2%) | 0.14 |
| Labs | | | | | | | 356,873 | 26,293 | |
| Lab values- HbA1c (%) ; n (%) | 64,253 (32.7%) | 4,705 (37.7%) | 10,520 (6.6%) | 752 (5.4%) | N/A | N/A | 74,773 (21.0%) | 5,457 (20.8%) | 0.00 |
| Lab values- HbA1c (%) (within 3 months); n (%) | 49,248 (25.0%) | 3,593 (28.8%) | 8,071 (5.0%) | 591 (4.3%) | N/A | N/A | 57,319 (16.1%) | 4,184 (15.9%) | 0.01 |
| Lab values- HbA1c (%) (within 6 months); n (%) | 64,253 (32.7%) | 4,705 (37.7%) | 10,520 (6.6%) | 752 (5.4%) | N/A | N/A | 74,773 (21.0%) | 5,457 (20.8%) | 0.00 |
| Lab values- BNP; n (%) | 1,407 (0.7%) | 128 (1.0%) | 199 (0.1%) | 24 (0.2%) | N/A | N/A | 1,606 (0.5%) | 152 (0.6%) | -0.01 |
| Lab values- BNP (within 3 months); n (%) | 867 (0.4%) | 84 (0.7%) | 137 (0.1%) | 21 (0.2%) | N/A | N/A | 1,004 (0.3%) | 105 (0.4%) | -0.02 |
| Lab values- BNP (within 6 months); n (%) | 1,407 (0.7%) | 128 (1.0%) | 199 (0.1%) | 24 (0.2%) | N/A | N/A | 1,606 (0.5%) | 152 (0.6%) | -0.01 |
| Lab values- BUN (mg/dl); n (%) | 65,450 (33.3%) | 4,847 (38.8%) | 7,968 (5.0%) | 784 (5.7%) | N/A | N/A | 73,418 (20.6%) | 5,631 (21.4%) | -0.02 |
| Lab values- BUN (mg/dl) (within 3 months); n (%) | 49,920 (25.4%) | 3,669 (29.4%) | 5,916 (3.7%) | 596 (4.3%) | N/A | N/A | 55,836 (15.6%) | 4,265 (16.2%) | -0.02 |
| Lab values- BUN (mg/dl) (within 6 months); n (%) | 65,450 (33.3%) | 4,847 (38.8%) | 7,968 (5.0%) | 784 (5.7%) | N/A | N/A | 73,418 (20.6%) | 5,631 (21.4%) | -0.02 |
| Lab values- Creatinine (mg/dl) ; n (%) | 66,968 (34.0%) | 5,002 (40.1%) | 8,308 (5.2%) | 816 (5.9%) | N/A | N/A | 75,276 (21.1%) | 5,818 (22.1%) | -0.02 |
| Lab values- Creatinine (mg/dl) (within 3 months) ; n (%) | 51,084 (26.0%) | 3,790 (30.4%) | 6,181 (3.9%) | 620 (4.5%) | N/A | N/A | 57,265 (16.0%) | 4,410 (16.8%) | -0.02 |
| Lab values- Creatinine (mg/dl) (within 6 months) ; n (%) | 66,968 (34.0%) | 5,002 (40.1%) | 8,308 (5.2%) | 816 (5.9%) | N/A | N/A | 75,276 (21.1%) | 5,818 (22.1%) | -0.02 |
| Lab values- HDL level (mg/dl); n (%) | 53,958 (27.4%) | 4,018 (32.2%) | 8,896 (5.6%) | 697 (5.0%) | N/A | N/A | 62,854 (17.6%) | 4,715 (17.9%) | -0.01 |
| Lab values- HDL level (mg/dl) (within 3 months); n (%) | 38,832 (19.7%) | 2,867 (23.0%) | 6,324 (3.9%) | 519 (3.8%) | N/A | N/A | 45,156 (12.7%) | 3,386 (12.9%) | -0.01 |
| Lab values- HDL level (mg/dl) (within 6 months); n (%) | 53,958 (27.4%) | 4,018 (32.2%) | 8,896 (5.6%) | 697 (5.0%) | N/A | N/A | 62,854 (17.6%) | 4,715 (17.9%) | -0.01 |
| Lab values- LDL level (mg/dl) ; n (%) | 55,693 (28.3%) | 4,146 (33.2%) | 9,674 (6.0%) | 720 (5.2%) | N/A | N/A | 65,367 (18.3%) | 4,866 (18.5%) | -0.01 |
| Lab values- LDL level (mg/dl) (within 3 months) ; n (%) | 40,047 (20.4%) | 2,966 (23.8%) | 6,888 (4.3%) | 531 (3.8%) | N/A | N/A | 46,935 (13.2%) | 3,497 (13.3%) | 0.00 |
| Lab values- LDL level (mg/dl) (within 6 months) ; n (%) | 55,693 (28.3%) | 4,146 (33.2%) | 9,674 (6.0%) | 720 (5.2%) | N/A | N/A | 65,367 (18.3%) | 4,866 (18.5%) | -0.01 |
| Lab values- NT-proBNP; n (%) | 178 (0.1%) | 30 (0.2%) | 15 (0.0%) | 3 (0.0%) | N/A | N/A | 193 (0.1%) | 33 (0.1%) | 0.00 |
| Lab values- NT-proBNP (within 3 months); n (%) | 108 (0.1%) | 20 (0.2%) | 8 (0.0%) | 1 (0.0%) | N/A | N/A | 116 (0.0%) | 21 (0.1%) | - |
| Lab values- NT-proBNP (within 6 months); n (%) | 178 (0.1%) | 30 (0.2%) | 15 (0.0%) | 3 (0.0%) | N/A | N/A | 193 (0.1%) | 33 (0.1%) | - |
| Lab values- Total cholesterol (mg/dl) ; n (%) | 54,700 (27.8%) | 4,119 (33.0%) | 9,020 (5.6%) | 707 (5.1%) | N/A | N/A | 63,720 (17.9%) | 4,826 (18.4%) | -0.01 |
| Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (%) | 39,389 (20.0%) | 2,940 (23.5%) | 6,388 (4.0%) | 528 (3.8%) | N/A | N/A | 45,777 (12.8%) | 3,468 (13.2%) | -0.01 |
| Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%) | 54,700 (27.8%) | 4,119 (33.0%) | 9,020 (5.6%) | 707 (5.1%) | N/A | N/A | 63,720 (17.9%) | 4,826 (18.4%) | -0.01 |
| Lab values- Triglyceride level (mg/dl); n (%) | 54,124 (27.5%) | 4,074 (32.6%) | 8,795 (5.5%) | 692 (5.0%) | N/A | N/A | 62,919 (17.6%) | 4,766 (18.1%) | -0.01 |
| Lab values- Triglyceride level (mg/dl) (within 3 months); n (%) | 39,010 (19.8%) | 2,913 (23.3%) | 6,245 (3.9%) | 514 (3.7%) | N/A | N/A | 45,255 (12.7%) | 3,427 (13.0%) | -0.01 |
| Lab values- Triglyceride level (mg/dl) (within 6 months); n (%) | 54,124 (27.5%) | 4,074 (32.6%) | 8,795 (5.5%) | 692 (5.0%) | N/A | N/A | 62,919 (17.6%) | 4,766 (18.1%) | -0.01 |
| Lab result number- HbA1c (%) mean (only 2 to 20 included) | 63,912 | 4,683 | 8,515 | 708 | N/A | N/A | 72,427 | 5,391 | |
| ...mean (sd) | 7.88 (1.69) | 7.88 (1.76) | 7.94 (1.76) | 7.85 (1.82) | N/A | N/A | 7.89 (1.70) | 7.88 (1.77) | 0.01 |
| ...median [IQR] | 7.50 [6.80, 8.55] | 7.45 [6.60, 8.80] | 7.50 [6.80, 8.60] | 7.40 [6.50, 8.80] | N/A | N/A | 7.50 (1.70) | 7.44 (1.77) | 0.03 |
| ...Missing; n (%) | 132,800 (67.5%) | 7,802 (62.5%) | 151,646 (94.7%) | 13,100 (94.9%) | N/A | N/A | 284,446 (79.7%) | 20,902 (79.5%) | 0.00 |
| Lab result number- BNP mean | 1,407 | 128 | 199 | 24 | N/A | N/A | 1,606 | 152 | |
| ...mean (sd) | 206.69 (379.43) | 104.88 (129.95) | 374.49 (927.73) | 112.61 (201.88) | N/A | N/A | 227.48 (482.27) | 106.10 (143.82) | 0.34 |
| ...median [IQR] | 91.10 [35.30, 238.60] | 48.85 [21.92, 141.45] | 83.67 [34.00, 320.00] | 27.00 [14.00, 134.95] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 195,305 (99.3%) | 12,357 (99.0%) | 159,962 (99.9%) | 13,784 (99.8%) | N/A | N/A | 355,267 (99.5%) | 26,141 (99.4%) | 0.01 |
| Lab result number- BUN (mg/dl) mean | 65,450 | 4,847 | 7,968 | 784 | N/A | N/A | 73,418 | 5,631 | |
| ...mean (sd) | 19.59 (8.55) | 18.99 (7.63) | 605.16 (9,769.77) | 681.77 (10,970.52) | N/A | N/A | 83.14 (3218.41) | 111.27 (4091.96) | -0.01 |
| ...median [IQR] | 18.00 [14.00, 23.00] | 17.50 [14.00, 22.00] | 17.12 [14.00, 22.50] | 17.17 [14.00, 22.00] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 131,262 (66.7%) | 7,638 (61.2%) | 152,193 (95.0%) | 13,024 (94.3%) | N/A | N/A | 283,455 (79.4%) | 20,662 (78.6%) | 0.02 |
| Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) | 66,538 | 4,972 | 7,775 | 746 | N/A | N/A | 74,313 | 5,718 | |
| ...mean (sd) | 1.08 (0.41) | 1.02 (0.36) | 1.06 (0.40) | 0.99 (0.30) | N/A | N/A | 1.08 (0.41) | 1.02 (0.35) | 0.16 |
| ...median [IQR] | 0.99 [0.82, 1.23] | 0.95 [0.78, 1.16] | 0.99 [0.82, 1.18] | 0.93 [0.78, 1.13] | N/A | N/A | 0.99 (0.41) | 0.95 (0.35) | 0.10 |
| ...Missing; n (%) | 130,174 (66.2%) | 7,513 (60.2%) | 152,386 (95.1%) | 13,062 (94.6%) | N/A | N/A | 282,560 (79.2%) | 20,575 (78.3%) | 0.02 |
| Lab result number- HDL level (mg/dl) mean (only <=5000 included) | 53,958 | 4,018 | 8,873 | 695 | N/A | N/A | 62,831 | 4,713 | |
| ...mean (sd) | 46.95 (13.91) | 46.76 (13.33) | 45.59 (47.34) | 44.84 (14.34) | N/A | N/A | 46.76 (21.97) | 46.48 (13.48) | 0.02 |
| ...median [IQR] | 45.00 [37.50, 54.00] | 45.00 [37.50, 54.00] | 44.00 [36.67, 52.00] | 43.50 [36.00, 53.00] | N/A | N/A | 44.86 (21.97) | 44.78 (13.48) | 0.00 |
| ...Missing; n (%) | 142,754 (72.6%) | 8,467 (67.8%) | 151,288 (94.5%) | 13,113 (95.0%) | N/A | N/A | 294,042 (82.4%) | 21,580 (82.1%) | 0.01 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|-------------------------|-------------------------|-------------------------|-------------------------|-------------------|-------------------|-------------------|-----------------|---------|
| Lab result number- LDL level (mg/dl) mean (only <=5000 included) | 54,466 | 4,060 | 8,748 | 635 | N/A | N/A | 63,214 | 4,695 | |
| ...mean (sd) | 87.59 (38.87) | 83.15 (38.01) | 88.66 (40.81) | 83.36 (41.13) | N/A | N/A | 87.74 (39.14) | 83.18 (38.45) | 0.12 |
| ...median [IQR] | 84.00 [63.50, 109.81] | 79.50 [60.54, 103.00] | 85.00 [64.50, 111.00] | 83.00 [62.00, 107.00] | N/A | N/A | 84.14 (39.14) | 79.97 (38.45) | 0.11 |
| ...Missing; n (%) | 142,246 (72.3%) | 8,425 (67.5%) | 151,413 (94.5%) | 13,173 (95.4%) | N/A | N/A | 293,659 (82.3%) | 21,598 (82.1%) | 0.01 |
| Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) | 54,656 | 4,118 | 8,992 | 704 | N/A | N/A | 63,648 | 4,822 | |
| ...mean (sd) | 172.55 (45.90) | 168.99 (44.50) | 172.40 (50.33) | 171.70 (49.20) | N/A | N/A | 172.53 (46.55) | 169.39 (45.22) | 0.07 |
| ...median [IQR] | 167.00 [142.00, 197.00] | 162.50 [140.00, 192.00] | 167.25 [142.00, 198.00] | 166.50 [143.00, 198.00] | N/A | N/A | 167.04 (46.55) | 163.08 (45.22) | 0.09 |
| ...Missing; n (%) | 142,056 (72.2%) | 8,367 (67.0%) | 151,169 (94.4%) | 13,104 (94.9%) | N/A | N/A | 293,225 (82.2%) | 21,471 (81.7%) | 0.01 |
| Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) | 54,122 | 4,074 | 8,770 | 690 | N/A | N/A | 62,892 | 4,764 | |
| ...mean (sd) | 177.75 (139.01) | 180.45 (141.28) | 182.37 (160.30) | 188.30 (138.00) | N/A | N/A | 178.39 (142.17) | 181.59 (140.82) | -0.02 |
| ...median [IQR] | 148.00 [106.00, 209.00] | 150.00 [108.00, 212.00] | 148.00 [105.00, 213.00] | 153.00 [108.00, 225.12] | N/A | N/A | 148.00 (142.17) | 150.43 (140.82) | -0.02 |
| ...Missing; n (%) | 142,590 (72.5%) | 8,411 (67.4%) | 151,391 (94.5%) | 13,118 (95.0%) | N/A | N/A | 293,981 (82.4%) | 21,529 (81.9%) | 0.01 |
| Lab result number- Hemoglobin mean (only >0 included) | 46,203 | 3,404 | 5,302 | 532 | N/A | N/A | 51,505 | 3,936 | |
| ...mean (sd) | 13.33 (1.71) | 13.48 (1.59) | 4,366.28 (194,400.62) | 302.76 (6,676.17) | N/A | N/A | 461.43 (62368.39) | 52.58 (2453.09) | 0.01 |
| ...median [IQR] | 13.40 [12.20, 14.50] | 13.50 [12.40, 14.50] | 13.50 [12.30, 14.60] | 13.50 [12.50, 14.60] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 150,509 (76.5%) | 9,081 (72.7%) | 154,859 (96.7%) | 13,276 (96.1%) | N/A | N/A | 305,368 (85.6%) | 22,357 (85.0%) | 0.02 |
| Lab result number- Serum sodium mean (only >90 and < 190 included) | 64,988 | 4,879 | 7,382 | 734 | N/A | N/A | 72,370 | 5,613 | |
| ...mean (sd) | 139.46 (2.82) | 139.80 (2.62) | 139.02 (2.67) | 139.17 (2.52) | N/A | N/A | 139.42 (2.81) | 139.72 (2.61) | -0.11 |
| ...median [IQR] | 140.00 [138.00, 141.00] | 140.00 [138.00, 141.50] | 139.00 [137.50, 141.00] | 139.00 [138.00, 141.00] | N/A | N/A | 139.90 (2.81) | 139.87 (2.61) | 0.01 |
| ...Missing; n (%) | 131,724 (67.0%) | 7,606 (60.9%) | 152,779 (95.4%) | 13,074 (94.7%) | N/A | N/A | 284,503 (79.7%) | 20,680 (78.7%) | 0.02 |
| Lab result number- Albumin mean (only >0 and <=10 included) | 59,908 | 4,526 | 6,409 | 689 | N/A | N/A | 66,317 | 5,215 | |
| ...mean (sd) | 4.22 (0.33) | 4.22 (0.30) | 4.14 (0.59) | 4.11 (0.62) | N/A | N/A | 4.21 (0.36) | 4.21 (0.36) | 0.00 |
| ...median [IQR] | 4.23 [4.00, 4.40] | 4.20 [4.00, 4.40] | 4.20 [4.00, 4.40] | 4.20 [4.00, 4.40] | N/A | N/A | 4.23 (0.36) | 4.20 (0.36) | 0.08 |
| ...Missing; n (%) | 136,804 (69.5%) | 7,959 (63.7%) | 153,752 (96.0%) | 13,119 (95.0%) | N/A | N/A | 290,556 (81.4%) | 21,078 (80.2%) | 0.03 |
| Lab result number- Glucose (fasting or random) mean (only 10-1000 included) | 64,902 | 4,876 | 7,253 | 722 | N/A | N/A | 72,155 | 5,598 | |
| ...mean (sd) | 165.03 (68.57) | 160.65 (68.99) | 169.17 (71.16) | 163.38 (68.72) | N/A | N/A | 165.45 (68.84) | 161.00 (68.96) | 0.06 |
| ...median [IQR] | 148.50 [121.00, 189.00] | 143.00 [113.00, 186.00] | 151.50 [122.00, 195.50] | 145.00 [114.38, 191.00] | N/A | N/A | 148.80 (68.84) | 143.26 (68.96) | 0.08 |
| ...Missing; n (%) | 131,810 (67.0%) | 7,609 (60.9%) | 152,908 (95.5%) | 13,086 (94.8%) | N/A | N/A | 284,718 (79.8%) | 20,695 (78.7%) | 0.03 |
| Lab result number- Potassium mean (only 1-7 included) | 66,412 | 4,964 | 7,815 | 768 | N/A | N/A | 74,227 | 5,732 | |
| ...mean (sd) | 4.45 (0.45) | 4.45 (0.42) | 4.37 (0.45) | 4.33 (0.46) | N/A | N/A | 4.44 (0.45) | 4.43 (0.43) | 0.02 |
| ...median [IQR] | 4.40 [4.17, 4.70] | 4.40 [4.20, 4.70] | 4.35 [4.05, 4.65] | 4.30 [4.00, 4.60] | N/A | N/A | 4.39 (0.45) | 4.39 (0.43) | 0.00 |
| ...Missing; n (%) | 130,300 (66.2%) | 7,521 (60.2%) | 152,346 (95.1%) | 13,040 (94.4%) | N/A | N/A | 282,646 (79.2%) | 20,561 (78.2%) | 0.02 |
| Comorbidity Scores | | | | | | | | | |
| CCI (180 days)- ICD9 and ICD10 | | | | | | | | | |
| ...mean (sd) | 2.83 (2.07) | 2.76 (1.84) | 2.22 (1.78) | 2.06 (1.51) | 3.18 (2.40) | 2.91 (2.02) | 2.94 (2.24) | 2.66 (1.86) | 0.14 |
| ...median [IQR] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 2.00 [1.00, 3.00] | 2.00 [1.00, 3.00] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 2.00 (2.24) | 2.00 (1.86) | 0.00 |
| Frailty Score: Qualitative Version 365 days as Categories, | | | | | | | | | |
| ...0; n (%) | 86,571 (44.0%) | 6,594 (52.8%) | 44,870 (28.0%) | 4,399 (31.9%) | 158,210 (27.7%) | 9,861 (34.6%) | 289,651 (31.2%) | 20,854 (38.1%) | -0.15 |
| ...1 to 2; n (%) | 66,596 (33.9%) | 3,860 (30.9%) | 69,481 (43.4%) | 6,189 (44.8%) | 191,508 (33.5%) | 9,366 (32.9%) | 327,585 (35.3%) | 19,415 (35.4%) | 0.00 |
| ...3 or more; n (%) | 43,545 (22.1%) | 2,031 (16.3%) | 45,810 (28.6%) | 3,220 (23.3%) | 221,750 (38.8%) | 9,284 (32.6%) | 311,105 (33.5%) | 14,535 (26.5%) | 0.15 |
| Frailty Score: Empirical Version 365 days as Categories, | | | | | | | | | |
| ...< 0.12908; n (%) | 37,724 (19.2%) | 2,178 (17.4%) | 25,919 (16.2%) | 2,299 (16.6%) | 52,677 (9.2%) | 2,579 (9.0%) | 116,320 (12.5%) | 7,056 (12.9%) | -0.01 |
| ...0.12908 - 0.1631167; n (%) | 63,072 (32.1%) | 3,967 (31.8%) | 51,002 (31.8%) | 4,561 (33.0%) | 127,292 (22.3%) | 6,775 (23.8%) | 241,366 (26.0%) | 15,303 (27.9%) | -0.04 |
| ...> 0.1631167; n (%) | 95,916 (48.8%) | 6,340 (50.8%) | 83,240 (52.0%) | 6,948 (50.3%) | 391,499 (68.5%) | 19,157 (67.2%) | 570,655 (61.5%) | 32,445 (59.2%) | 0.05 |
| Non-Frailty; n (%) | 111,432 (56.6%) | 7,721 (61.8%) | 81,246 (50.7%) | 7,771 (56.3%) | 25,833 (4.5%) | 1,177 (4.1%) | 218,511 (23.5%) | 16,669 (30.4%) | -0.16 |
| Frailty Score (mean): Qualitative Version 365 days, | | | | | | | | | |
| ...mean (sd) | 1.50 (2.05) | 1.11 (1.65) | 1.90 (2.04) | 1.58 (1.65) | 2.46 (2.61) | 1.97 (2.22) | 2.16 (2.41) | 1.68 (1.97) | 0.22 |
| ...median [IQR] | 1.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 1.00 [0.00, 3.00] | 1.00 [0.00, 2.00] | 2.00 [0.00, 4.00] | 1.00 [0.00, 3.00] | 1.62 (2.41) | 0.77 (1.97) | 0.39 |
| Frailty Score (mean): Empirical Version 365 days, | | | | | | | | | |
| ...mean (sd) | 0.17 (0.06) | 0.17 (0.05) | 0.17 (0.05) | 0.17 (0.05) | 0.21 (0.08) | 0.20 (0.07) | 0.19 (0.07) | 0.19 (0.06) | 0.00 |
| ...median [IQR] | 0.16 [0.14, 0.20] | 0.16 [0.14, 0.20] | 0.16 [0.13, 0.19] | 0.16 [0.13, 0.19] | 0.19 [0.15, 0.24] | 0.19 [0.15, 0.23] | 0.18 (0.07) | 0.18 (0.06) | 0.00 |
| Healthcare Utilization | | | | | | | | | |
| Any hospitalization; n (%) | 22,822 (11.6%) | 932 (7.5%) | 22,913 (14.3%) | 1,089 (7.9%) | 94,431 (16.5%) | 2,641 (9.3%) | 140,166 (15.1%) | 4,662 (8.5%) | 0.21 |
| Any hospitalization within prior 30 days; n (%) | 8,976 (4.6%) | 186 (1.5%) | 7,999 (5.0%) | 174 (1.3%) | 34,791 (6.1%) | 501 (1.8%) | 51,766 (5.6%) | 861 (1.6%) | 0.22 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|--------------------|---------------------|--------------------|---------------------|--------------------|---------------------|-----------------|----------------|-------|
| Any hospitalization during prior 31-180 days; n (%) | 15,333 (7.8%) | 789 (6.3%) | 16,116 (10.1%) | 941 (6.8%) | 68,046 (11.9%) | 2,248 (7.9%) | 99,495 (10.7%) | 3,978 (7.3%) | 0.12 |
| Endocrinologist Visit; n (%) | 10,612 (5.4%) | 2,709 (21.7%) | 9,104 (5.7%) | 3,114 (22.6%) | 39,543 (6.9%) | 7,223 (25.3%) | 59,259 (6.4%) | 13,046 (23.8%) | -0.50 |
| Endocrinologist Visit (30 days prior); n (%) | 5,832 (3.0%) | 1,706 (13.7%) | 5,126 (3.2%) | 2,086 (15.1%) | 21,478 (3.8%) | 4,455 (15.6%) | 32,436 (3.5%) | 8,247 (15.0%) | -0.40 |
| Endocrinologist Visit (31 to 180 days prior); n (%) | 7,605 (3.9%) | 2,033 (16.3%) | 6,514 (4.1%) | 2,270 (16.4%) | 29,932 (5.2%) | 5,602 (19.6%) | 44,051 (4.7%) | 9,905 (18.1%) | -0.43 |
| Internal medicine/family medicine visits; n (%) | 174,004 (88.5%) | 10,331 (82.7%) | 134,865 (84.2%) | 11,859 (85.9%) | 484,478 (84.8%) | 23,819 (83.5%) | 793,347 (85.5%) | 46,009 (84.0%) | 0.04 |
| Internal medicine/family medicine visits (30 days prior); n (%) | 130,177 (66.2%) | 7,189 (57.6%) | 98,733 (61.6%) | 8,352 (60.5%) | 347,640 (60.8%) | 15,622 (54.8%) | 576,550 (62.1%) | 31,163 (56.9%) | 0.11 |
| Internal medicine/family medicine visits (31 to 180 days prior); n (%) | 153,193 (77.9%) | 9,462 (75.8%) | 117,762 (73.5%) | 10,731 (77.7%) | 424,882 (74.3%) | 21,819 (76.5%) | 695,837 (75.0%) | 42,012 (76.7%) | -0.04 |
| Cardiologist visit; n (%) | 61,106 (31.1%) | 4,345 (34.8%) | 46,909 (29.3%) | 4,666 (33.8%) | 217,811 (38.1%) | 10,584 (37.1%) | 325,826 (35.1%) | 19,595 (35.8%) | -0.01 |
| Number of Cardiologist visits (30 days prior); n (%) | 23,285 (11.8%) | 1,441 (11.5%) | 17,006 (10.6%) | 1,545 (11.2%) | 81,708 (14.3%) | 3,371 (11.8%) | 121,999 (13.1%) | 6,357 (11.6%) | 0.05 |
| Number of Cardiologist visits (31 to 180 days prior); n (%) | 50,549 (25.7%) | 3,740 (30.0%) | 39,491 (24.7%) | 4,016 (29.1%) | 185,317 (32.4%) | 9,345 (32.8%) | 275,357 (29.7%) | 17,101 (31.2%) | -0.03 |
| Electrocardiogram ; n (%) | 66,713 (33.9%) | 4,279 (34.3%) | 58,412 (36.5%) | 5,031 (36.4%) | 220,597 (38.6%) | 10,338 (36.3%) | 345,722 (37.2%) | 19,648 (35.9%) | 0.03 |
| Use of glucose test strips; n (%) | 7,094 (3.6%) | 514 (4.1%) | 5,465 (3.4%) | 626 (4.5%) | 19,740 (3.5%) | 1,110 (3.9%) | 32,299 (3.5%) | 2,250 (4.1%) | -0.03 |
| Dialysis; n (%) | 117 (0.1%) | 8 (0.1%) | 144 (0.1%) | 6 (0.0%) | 647 (0.1%) | 11 (0.0%) | 908 (0.1%) | 025 (0.0%) | 0.04 |
| Naive new user v8 ; n (%) | 59,575 (30.3%) | 2,843 (22.8%) | 47,064 (29.4%) | 2,515 (18.2%) | 153,729 (26.9%) | 4,885 (17.1%) | 260,368 (28.0%) | 10,243 (18.7%) | 0.22 |
| N antidiabetic drugs at index date | | | | | | | | | |
| ...mean (sd) | 1.67 (0.62) | 1.75 (0.72) | 1.69 (0.65) | 1.77 (0.75) | 1.65 (0.62) | 1.78 (0.71) | 1.66 (0.63) | 1.77 (0.72) | -0.16 |
| ...median [IQR] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 (0.63) | 2.00 (0.72) | 0.00 |
| number of different/distinct medication prescriptions | | | | | | | | | |
| ...mean (sd) | 9.22 (4.44) | 11.19 (5.24) | 9.31 (4.45) | 11.10 (4.95) | 9.61 (4.49) | 11.07 (4.88) | 9.48 (4.47) | 11.10 (4.98) | -0.34 |
| ...median [IQR] | 9.00 [6.00, 12.00] | 11.00 [8.00, 14.00] | 9.00 [6.00, 12.00] | 11.00 [8.00, 14.00] | 9.00 [6.00, 12.00] | 10.00 [8.00, 14.00] | 9.00 (4.47) | 10.48 (4.98) | -0.31 |
| Number of Hospitalizations | | | | | | | | | |
| ...mean (sd) | 0.14 (0.45) | 0.09 (0.34) | 0.17 (0.46) | 0.09 (0.33) | 0.23 (0.62) | 0.12 (0.41) | 0.20 (0.56) | 0.11 (0.38) | 0.19 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.56) | 0.00 (0.38) | 0.00 |
| Number of hospital days | | | | | | | | | |
| ...mean (sd) | 0.86 (3.80) | 0.45 (2.50) | 1.02 (4.23) | 0.43 (2.24) | 1.61 (5.91) | 0.69 (3.22) | 1.35 (5.26) | 0.57 (2.84) | 0.18 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (5.26) | 0.00 (2.84) | 0.00 |
| Number of Emergency Department (ED) visits | | | | | | | | | |
| ...mean (sd) | 0.47 (1.33) | 0.40 (1.19) | 0.27 (1.64) | 0.14 (1.20) | 0.69 (1.57) | 0.46 (1.22) | 0.57 (1.53) | 0.37 (1.21) | 0.14 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 0.00] | 0.00 (1.53) | 0.00 (1.21) | 0.00 |
| Number of Office visits | | | | | | | | | |
| ...mean (sd) | 4.71 (3.74) | 5.85 (4.16) | 5.01 (4.03) | 6.08 (4.35) | 5.31 (4.32) | 6.61 (4.77) | 5.13 (4.15) | 6.30 (4.53) | -0.27 |
| ...median [IQR] | 4.00 [2.00, 6.00] | 5.00 [3.00, 8.00] | 4.00 [2.00, 7.00] | 5.00 [3.00, 8.00] | 4.00 [2.00, 7.00] | 6.00 [3.00, 9.00] | 4.00 (4.15) | 5.52 (4.53) | -0.35 |
| Number of Endocrinologist visits | | | | | | | | | |
| ...mean (sd) | 0.24 (1.59) | 1.18 (3.75) | 0.25 (1.57) | 1.22 (3.84) | 0.38 (2.33) | 1.74 (5.44) | 0.33 (2.07) | 1.48 (4.72) | -0.32 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 (2.07) | 0.00 (4.72) | 0.00 |
| Number of internal medicine/family medicine visits | | | | | | | | | |
| ...mean (sd) | 10.56 (13.70) | 10.28 (14.77) | 7.25 (9.99) | 7.76 (9.80) | 8.78 (11.47) | 8.76 (11.54) | 8.89 (11.75) | 8.85 (11.97) | 0.00 |
| ...median [IQR] | 6.00 [2.00, 14.00] | 6.00 [2.00, 13.00] | 4.00 [2.00, 9.00] | 5.00 [2.00, 10.00] | 5.00 [2.00, 12.00] | 5.00 [2.00, 12.00] | 5.04 (11.75) | 5.23 (11.97) | -0.02 |
| Number of Cardiologist visits | | | | | | | | | |
| ...mean (sd) | 1.59 (4.13) | 1.69 (3.99) | 1.34 (3.54) | 1.56 (3.83) | 2.16 (5.18) | 2.04 (5.04) | 1.90 (4.72) | 1.84 (4.53) | 0.01 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 (4.72) | 0.00 (4.53) | 0.00 |
| Number electrocardiograms received | | | | | | | | | |
| ...mean (sd) | 0.71 (1.57) | 0.67 (1.46) | 0.69 (1.33) | 0.64 (1.22) | 0.86 (1.63) | 0.72 (1.36) | 0.80 (1.57) | 0.69 (1.35) | 0.08 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 (1.57) | 0.00 (1.35) | 0.00 |
| Number of HbA1c tests ordered | | | | | | | | | |
| ...mean (sd) | 1.18 (0.89) | 1.37 (0.92) | 0.86 (0.89) | 1.14 (0.94) | 1.27 (0.87) | 1.50 (0.88) | 1.18 (0.88) | 1.38 (0.90) | -0.22 |
| ...median [IQR] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 [0.00, 1.00] | 1.00 [0.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 (0.88) | 1.00 (0.90) | 0.00 |
| Number of glucose tests ordered | | | | | | | | | |
| ...mean (sd) | 0.47 (2.36) | 0.58 (1.39) | 0.38 (1.34) | 0.49 (1.14) | 0.39 (1.02) | 0.53 (1.18) | 0.41 (1.46) | 0.53 (1.22) | -0.09 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 (1.46) | 0.00 (1.22) | 0.00 |
| Number of lipid tests ordered | | | | | | | | | |
| ...mean (sd) | 0.94 (0.93) | 1.08 (1.02) | 0.74 (1.19) | 1.00 (1.28) | 0.93 (0.82) | 1.11 (0.90) | 0.90 (0.92) | 1.08 (1.03) | -0.18 |
| ...median [IQR] | 1.00 [0.00, 1.00] | 1.00 [0.00, 2.00] | 0.00 [0.00, 1.00] | 1.00 [0.00, 2.00] | 1.00 [0.00, 1.00] | 1.00 [1.00, 2.00] | 0.83 (0.92) | 1.00 (1.03) | -0.17 |
| Number of creatinine tests ordered | | | | | | | | | |
| ...mean (sd) | 0.07 (0.35) | 0.06 (0.32) | 0.10 (0.50) | 0.07 (0.35) | 0.09 (0.42) | 0.10 (0.40) | 0.09 (0.42) | 0.08 (0.37) | 0.03 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.42) | 0.00 (0.37) | 0.00 |
| Number of BUN tests ordered | | | | | | | | | |
| ...mean (sd) | 0.04 (0.28) | 0.03 (0.24) | 0.06 (0.37) | 0.04 (0.29) | 0.06 (0.34) | 0.06 (0.30) | 0.06 (0.33) | 0.05 (0.28) | 0.03 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.33) | 0.00 (0.28) | 0.00 |
| Number of tests for microalbuminuria | | | | | | | | | |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|-------------------|--------------------|-------------------|-------------------|-------------------|--------------------|-----------------|----------------|-------|
| ...mean (sd) | 0.71 (1.13) | 0.85 (1.24) | 0.44 (0.90) | 0.63 (1.06) | 0.41 (0.68) | 0.56 (0.78) | 0.48 (0.83) | 0.64 (0.97) | -0.18 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 (0.83) | 0.00 (0.97) | 0.00 |
| Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level | | | | | | | | | |
| ...mean (sd) | 5.56 (7.93) | 7.14 (8.40) | 2.46 (5.45) | 2.45 (4.54) | 6.43 (9.60) | 6.71 (8.93) | 5.56 (8.67) | 5.73 (7.92) | -0.02 |
| ...median [IQR] | 3.00 [0.00, 8.00] | 5.00 [0.00, 11.00] | 0.00 [0.00, 3.00] | 0.00 [0.00, 4.00] | 3.00 [0.00, 9.00] | 4.00 [0.00, 10.00] | 2.48 (8.67) | 3.22 (7.92) | -0.09 |
| | | | | | | | | | |
| Use of thiazide; n (%) | 27,419 (13.9%) | 1,625 (13.0%) | 21,582 (13.5%) | 1,717 (12.4%) | 84,834 (14.8%) | 4,198 (14.7%) | 133,835 (14.4%) | 7,540 (13.8%) | 0.02 |
| Use of beta blockers; n (%) | 85,663 (43.5%) | 5,416 (43.4%) | 74,450 (46.5%) | 6,002 (43.5%) | 283,394 (49.6%) | 13,479 (47.3%) | 443,507 (47.8%) | 24,897 (45.4%) | 0.05 |
| Use of calcium channel blockers; n (%) | 62,900 (32.0%) | 3,589 (28.7%) | 50,730 (31.7%) | 3,915 (28.4%) | 199,227 (34.9%) | 8,767 (30.7%) | 312,857 (33.7%) | 16,271 (29.7%) | 0.09 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| PS-matched | | | | | | | | | |
|---|----------------------------------|-----------------------|----------------------------------|-----------------------|----------------------------------|-----------------------|----------------------------------|-----------------------|-----------|
| | Optum | | MarketScan | | Medicare | | POOLED | | |
| Variable | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | Reference- 2nd Generation SUs | Exposure- Liraglutide | St. Diff. |
| Number of patients | 12253 | 12253 | 13591 | 13591 | 28338 | 28338 | 54,182 | 54,182 | |
| Age | | | | | | | | | |
| ...mean (sd) | 65.57 (7.08) | 65.79 (6.77) | 62.61 (6.66) | 62.89 (6.12) | 70.39 (5.17) | 70.55 (4.99) | 67.35 (6.04) | 67.55 (5.73) | -0.03 |
| ...median [IQR] | 66.00 [61.00, 70.00] | 66.00 [61.00, 70.00] | 62.00 [60.00, 65.00] | 62.00 [60.00, 65.00] | 69.00 [66.00, 73.00] | 69.00 [67.00, 73.00] | 66.57 (6.04) | 66.57 (5.73) | 0.00 |
| Age categories | | | | | | | | | |
| ...18 - 54; n (%) | 856 (7.0%) | 700 (5.7%) | 1,433 (10.5%) | 1,145 (8.4%) | 0 (0.0%) | 0 (0.0%) | 2,289 (4.2%) | 1,845 (3.4%) | 0.04 |
| ...55 - 64; n (%) | 4,440 (36.2%) | 4,474 (36.5%) | 8,439 (62.1%) | 8,448 (62.2%) | 876 (3.1%) | 682 (2.4%) | 13,755 (25.4%) | 13,604 (25.1%) | 0.01 |
| ...65 - 74; n (%) | 5,664 (46.2%) | 5,858 (47.8%) | 2,893 (21.3%) | 3,298 (24.3%) | 22,136 (78.1%) | 22,229 (78.4%) | 30,693 (56.6%) | 31,385 (57.9%) | -0.03 |
| ...≥ 75; n (%) | 1,293 (10.6%) | 1,221 (10.0%) | 826 (6.1%) | 700 (5.2%) | 5,326 (18.8%) | 5,427 (19.2%) | 7,445 (13.7%) | 7,348 (13.6%) | 0.00 |
| Gender | | | | | | | | | |
| ...Males; n (%) | 5,550 (45.3%) | 5,514 (45.0%) | 6,577 (48.4%) | 6,643 (48.9%) | 11,978 (42.3%) | 11,972 (42.2%) | 24,105 (44.5%) | 24,129 (44.5%) | 0.00 |
| ...Females; n (%) | 6,703 (54.7%) | 6,739 (55.0%) | 7,014 (51.6%) | 6,948 (51.1%) | 16,360 (57.7%) | 16,366 (57.8%) | 30,077 (55.5%) | 30,053 (55.5%) | 0.00 |
| Race | | | | | | | | | |
| ...White; n (%) | N/A | N/A | N/A | N/A | 24,117 (85.1%) | 23,930 (84.4%) | 24,117 (85.1%) | 23,930 (84.4%) | 0.02 |
| ...Black; n (%) | N/A | N/A | N/A | N/A | 2,464 (8.7%) | 2,557 (9.0%) | 2,464 (8.7%) | 2,557 (9.0%) | -0.01 |
| ...Asian; n (%) | N/A | N/A | N/A | N/A | 364 (1.3%) | 380 (1.3%) | 364 (1.3%) | 380 (1.3%) | 0.00 |
| ...Hispanic; n (%) | N/A | N/A | N/A | N/A | 481 (1.7%) | 511 (1.8%) | 481 (1.7%) | 511 (1.8%) | -0.01 |
| ...North American Native; n (%) | N/A | N/A | N/A | N/A | 89 (0.3%) | 122 (0.4%) | 89 (0.3%) | 122 (0.4%) | -0.02 |
| ...Other/Unknown; n (%) | N/A | N/A | N/A | N/A | 823 (2.9%) | 838 (3.0%) | 823 (2.9%) | 838 (3.0%) | -0.01 |
| Region (lumping missing&other category with West) | | | | | | | | | |
| ...Northeast; n (%) | 1,166 (9.5%) | 1,177 (9.6%) | 2,666 (19.6%) | 2,729 (20.1%) | 4,555 (16.1%) | 4,669 (16.5%) | 8,387 (15.5%) | 8,575 (15.8%) | -0.01 |
| ...South; n (%) | 6,705 (54.7%) | 6,635 (54.2%) | 2,735 (20.1%) | 2,766 (20.4%) | 13,129 (46.3%) | 13,013 (45.9%) | 22,569 (41.7%) | 22,414 (41.4%) | 0.01 |
| ...Midwest; n (%) | 2,289 (18.7%) | 2,291 (18.7%) | 6,666 (49.0%) | 6,500 (47.8%) | 6,131 (21.6%) | 6,116 (21.6%) | 15,086 (27.8%) | 14,907 (27.5%) | 0.01 |
| ...West; n (%) | 2,093 (17.1%) | 2,150 (17.5%) | 1,372 (10.1%) | 1,439 (10.6%) | 4,523 (16.0%) | 4,540 (16.0%) | 7,988 (14.7%) | 8,129 (15.0%) | -0.01 |
| ...Unknown+missing; n (%) | N/A | N/A | 152 (1.1%) | 157 (1.2%) | N/A | N/A | 152 (1.1%) | 157 (1.2%) | -0.01 |
| CV Covariates | | | | | | | | | |
| Ischemic heart disease; n (%) | 3,626 (29.6%) | 3,604 (29.4%) | 4,206 (30.9%) | 4,351 (32.0%) | 8,731 (30.8%) | 8,831 (31.2%) | 16,563 (30.6%) | 16,786 (31.0%) | -0.01 |
| Acute MI; n (%) | 177 (1.4%) | 170 (1.4%) | 192 (1.4%) | 210 (1.5%) | 328 (1.2%) | 334 (1.2%) | 697 (1.3%) | 714 (1.3%) | 0.00 |
| ACS/unstable angina; n (%) | 234 (1.9%) | 254 (2.1%) | 271 (2.0%) | 281 (2.1%) | 511 (1.8%) | 477 (1.7%) | 1,016 (1.9%) | 1,012 (1.9%) | 0.00 |
| Old MI; n (%) | 485 (4.0%) | 479 (3.9%) | 279 (2.1%) | 288 (2.1%) | 1,043 (3.7%) | 1,034 (3.6%) | 1,807 (3.3%) | 1,801 (3.3%) | 0.00 |
| Stable angina; n (%) | 552 (4.5%) | 583 (4.8%) | 475 (3.5%) | 488 (3.6%) | 1,057 (3.7%) | 1,123 (4.0%) | 2,084 (3.8%) | 2,194 (4.0%) | -0.01 |
| Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%) | 3,397 (27.7%) | 3,383 (27.6%) | 3,991 (29.4%) | 4,144 (30.5%) | 8,336 (29.4%) | 8,421 (29.7%) | 15,724 (29.0%) | 15,948 (29.4%) | -0.01 |
| Other atherosclerosis with ICD10 ; n (%) | 111 (0.9%) | 119 (1.0%) | 139 (1.0%) | 155 (1.1%) | 443 (1.6%) | 470 (1.7%) | 693 (1.3%) | 744 (1.4%) | -0.01 |
| Previous cardiac procedure (CABG or PTCA or Stent); n (%) | 88 (0.7%) | 96 (0.8%) | 125 (0.9%) | 137 (1.0%) | 174 (0.6%) | 140 (0.5%) | 387 (0.7%) | 373 (0.7%) | 0.00 |
| History of CABG or PTCA; n (%) | 868 (7.1%) | 896 (7.3%) | 548 (4.0%) | 566 (4.2%) | 2,354 (8.3%) | 2,366 (8.3%) | 3,770 (7.0%) | 3,828 (7.1%) | 0.00 |
| Any stroke; n (%) | 925 (7.5%) | 891 (7.3%) | 958 (7.0%) | 1,002 (7.4%) | 2,454 (8.7%) | 2,433 (8.6%) | 4,337 (8.0%) | 4,326 (8.0%) | 0.00 |
| Ischemic stroke (w and w/o mention of cerebral infarction); n (%) | 912 (7.4%) | 886 (7.2%) | 938 (6.9%) | 985 (7.2%) | 2,437 (8.6%) | 2,410 (8.5%) | 4,287 (7.9%) | 4,281 (7.9%) | 0.00 |
| Hemorrhagic stroke; n (%) | 19 (0.2%) | 16 (0.1%) | 27 (0.2%) | 27 (0.2%) | 38 (0.1%) | 45 (0.2%) | 084 (0.2%) | 088 (0.2%) | 0.00 |
| TIA; n (%) | 229 (1.9%) | 224 (1.8%) | 234 (1.7%) | 239 (1.8%) | 516 (1.8%) | 511 (1.8%) | 979 (1.8%) | 974 (1.8%) | 0.00 |
| Other cerebrovascular disease; n (%) | 182 (1.5%) | 225 (1.8%) | 182 (1.3%) | 164 (1.2%) | 615 (2.2%) | 583 (2.1%) | 979 (1.8%) | 972 (1.8%) | 0.00 |
| Late effects of cerebrovascular disease; n (%) | 146 (1.2%) | 143 (1.2%) | 97 (0.7%) | 92 (0.7%) | 382 (1.3%) | 415 (1.5%) | 625 (1.2%) | 650 (1.2%) | 0.00 |
| Cerebrovascular procedure; n (%) | 14 (0.1%) | 12 (0.1%) | 10 (0.1%) | 11 (0.1%) | 35 (0.1%) | 25 (0.1%) | 059 (0.1%) | 048 (0.1%) | 0.00 |
| Heart failure (CHF); n (%) | 1,220 (10.0%) | 1,238 (10.1%) | 978 (7.2%) | 976 (7.2%) | 3,335 (11.8%) | 3,322 (11.7%) | 5,533 (10.2%) | 5,536 (10.2%) | 0.00 |
| Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%) | 1,032 (8.4%) | 1,076 (8.8%) | 1,066 (7.8%) | 1,057 (7.8%) | 2,898 (10.2%) | 2,934 (10.4%) | 4,996 (9.2%) | 5,067 (9.4%) | -0.01 |
| Atrial fibrillation; n (%) | 927 (7.6%) | 947 (7.7%) | 769 (5.7%) | 774 (5.7%) | 3,069 (10.8%) | 3,058 (10.8%) | 4,765 (8.8%) | 4,779 (8.8%) | 0.00 |
| Other cardiac dysrhythmia; n (%) | 1,257 (10.3%) | 1,284 (10.5%) | 896 (6.6%) | 925 (6.8%) | 3,317 (11.7%) | 3,335 (11.8%) | 5,470 (10.1%) | 5,544 (10.2%) | 0.00 |
| Cardiac conduction disorders; n (%) | 349 (2.8%) | 350 (2.9%) | 228 (1.7%) | 281 (2.1%) | 1,094 (3.9%) | 1,069 (3.8%) | 1,671 (3.1%) | 1,700 (3.1%) | 0.00 |
| Other CVD; n (%) | 1,446 (11.8%) | 1,455 (11.9%) | 1,455 (10.7%) | 1,447 (10.6%) | 4,255 (15.0%) | 4,141 (14.6%) | 7,156 (13.2%) | 7,043 (13.0%) | 0.01 |
| Diabetes-related complications | | | | | | | | | |
| Diabetic retinopathy; n (%) | 828 (6.8%) | 904 (7.4%) | 613 (4.5%) | 641 (4.7%) | 2,266 (8.0%) | 2,359 (8.3%) | 3,707 (6.8%) | 3,904 (7.2%) | -0.02 |
| Diabetes with other ophthalmic manifestations; n (%) | 85 (0.7%) | 90 (0.7%) | 398 (2.9%) | 440 (3.2%) | 834 (2.9%) | 867 (3.1%) | 1,317 (2.4%) | 1,397 (2.6%) | -0.01 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|---------|
| Retinal detachment, vitreous hemorrhage, vitrectomy; n (%) | 55 (0.4%) | 53 (0.4%) | 48 (0.4%) | 46 (0.3%) | 144 (0.5%) | 135 (0.5%) | 247 (0.5%) | 234 (0.4%) | 0.01 |
| Retinal laser coagulation therapy; n (%) | 70 (0.6%) | 71 (0.6%) | 82 (0.6%) | 91 (0.7%) | 190 (0.7%) | 199 (0.7%) | 342 (0.6%) | 361 (0.7%) | -0.01 |
| Occurrence of Diabetic Neuropathy ; n (%) | 2,907 (23.7%) | 2,874 (23.5%) | 1,852 (13.6%) | 1,890 (13.9%) | 6,479 (22.9%) | 6,619 (23.4%) | 11,238 (20.7%) | 11,383 (21.0%) | -0.01 |
| Occurrence of diabetic nephropathy with ICD10 ; n (%) | 2,029 (16.6%) | 2,102 (17.2%) | 1,042 (7.7%) | 1,008 (7.4%) | 3,374 (11.9%) | 3,490 (12.3%) | 6,445 (11.9%) | 6,600 (12.2%) | -0.01 |
| Hypoglycemia ; n (%) | 267 (2.2%) | 271 (2.2%) | 369 (2.7%) | 400 (2.9%) | 866 (3.1%) | 840 (3.0%) | 1,502 (2.8%) | 1,511 (2.8%) | 0.00 |
| Hyperglycemia; n (%) | 563 (4.6%) | 561 (4.6%) | 425 (3.1%) | 424 (3.1%) | 1,251 (4.4%) | 1,233 (4.4%) | 2,239 (4.1%) | 2,218 (4.1%) | 0.00 |
| Disorders of fluid electrolyte and acid-base balance; n (%) | 766 (6.3%) | 812 (6.6%) | 603 (4.4%) | 592 (4.4%) | 2,084 (7.4%) | 2,147 (7.6%) | 3,453 (6.4%) | 3,551 (6.6%) | -0.01 |
| Diabetic ketoacidosis; n (%) | 16 (0.1%) | 14 (0.1%) | 19 (0.1%) | 15 (0.1%) | 31 (0.1%) | 32 (0.1%) | 066 (0.1%) | 061 (0.1%) | 0.00 |
| Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%) | 61 (0.5%) | 68 (0.6%) | 41 (0.3%) | 44 (0.3%) | 122 (0.4%) | 125 (0.4%) | 224 (0.4%) | 237 (0.4%) | 0.00 |
| Diabetes with peripheral circulatory disorders with ICD-10 ; n (%) | 950 (7.8%) | 959 (7.8%) | 497 (3.7%) | 522 (3.8%) | 1,985 (7.0%) | 2,021 (7.1%) | 3,432 (6.3%) | 3,502 (6.5%) | -0.01 |
| Diabetic Foot; n (%) | 309 (2.5%) | 308 (2.5%) | 275 (2.0%) | 296 (2.2%) | 909 (3.2%) | 931 (3.3%) | 1,493 (2.8%) | 1,535 (2.8%) | 0.00 |
| Gangrene ; n (%) | 35 (0.3%) | 33 (0.3%) | 24 (0.2%) | 20 (0.1%) | 53 (0.2%) | 60 (0.2%) | 112 (0.2%) | 113 (0.2%) | 0.00 |
| Lower extremity amputation; n (%) | 114 (0.9%) | 103 (0.8%) | 39 (0.3%) | 41 (0.3%) | 153 (0.5%) | 163 (0.6%) | 306 (0.6%) | 307 (0.6%) | 0.00 |
| Osteomyelitis; n (%) | 112 (0.9%) | 87 (0.7%) | 71 (0.5%) | 66 (0.5%) | 196 (0.7%) | 166 (0.6%) | 379 (0.7%) | 319 (0.6%) | 0.01 |
| Skin infections ; n (%) | 693 (5.7%) | 714 (5.8%) | 788 (5.8%) | 794 (5.8%) | 2,223 (7.8%) | 2,241 (7.9%) | 3,704 (6.8%) | 3,749 (6.9%) | 0.00 |
| Erectile dysfunction; n (%) | 353 (2.9%) | 350 (2.9%) | 307 (2.3%) | 312 (2.3%) | 833 (2.9%) | 821 (2.9%) | 1,493 (2.8%) | 1,483 (2.7%) | 0.01 |
| Diabetes with unspecified complication; n (%) | 742 (6.1%) | 789 (6.4%) | 634 (4.7%) | 634 (4.7%) | 1,595 (5.6%) | 1,646 (5.8%) | 2,971 (5.5%) | 3,069 (5.7%) | -0.01 |
| Diabetes mellitus without mention of complications; n (%) | 10,682 (87.2%) | 10,639 (86.8%) | 12,694 (93.4%) | 12,712 (93.5%) | 26,299 (92.8%) | 26,320 (92.9%) | 49,675 (91.7%) | 49,671 (91.7%) | 0.00 |
| Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%) | 11,668 (95.2%) | 11,662 (95.2%) | 12,150 (89.4%) | 12,086 (88.9%) | 27,462 (96.9%) | 27,458 (96.9%) | 51,280 (94.6%) | 51,206 (94.5%) | 0.00 |
| Hyperlipidemia ; n (%) | 9,662 (78.9%) | 9,646 (78.7%) | 9,610 (70.7%) | 9,643 (71.0%) | 23,411 (82.6%) | 23,471 (82.8%) | 42,683 (78.8%) | 42,760 (78.9%) | 0.00 |
| Edema; n (%) | 1,043 (8.5%) | 1,052 (8.6%) | 801 (5.9%) | 818 (6.0%) | 3,069 (10.8%) | 3,179 (11.2%) | 4,913 (9.1%) | 5,049 (9.3%) | -0.01 |
| Renal Dysfunction (non-diabetic) ; n (%) | 2,712 (22.1%) | 2,829 (23.1%) | 1,804 (13.3%) | 1,850 (13.6%) | 6,163 (21.7%) | 6,236 (22.0%) | 10,679 (19.7%) | 10,915 (20.1%) | -0.01 |
| Occurrence of acute renal disease ; n (%) | 378 (3.1%) | 362 (3.0%) | 199 (1.5%) | 212 (1.6%) | 922 (3.3%) | 902 (3.2%) | 1,499 (2.8%) | 1,476 (2.7%) | 0.01 |
| Occurrence of chronic renal insufficiency; n (%) | 2,280 (18.6%) | 2,425 (19.8%) | 1,368 (10.1%) | 1,413 (10.4%) | 5,213 (18.4%) | 5,351 (18.9%) | 8,861 (16.4%) | 9,189 (17.0%) | -0.02 |
| Chronic kidney disease ; n (%) | 2,222 (18.1%) | 2,351 (19.2%) | 1,305 (9.6%) | 1,356 (10.0%) | 4,960 (17.5%) | 5,072 (17.9%) | 8,487 (15.7%) | 8,779 (16.2%) | -0.01 |
| CKD Stage 3-4; n (%) | 1,662 (13.6%) | 1,694 (13.8%) | 967 (7.1%) | 1,002 (7.4%) | 3,531 (12.5%) | 3,647 (12.9%) | 6,160 (11.4%) | 6,343 (11.7%) | -0.01 |
| Occurrence of hypertensive nephropathy; n (%) | 996 (8.1%) | 1,051 (8.6%) | 517 (3.8%) | 517 (3.8%) | 2,208 (7.8%) | 2,249 (7.9%) | 3,721 (6.9%) | 3,817 (7.0%) | 0.00 |
| Occurrence of miscellaneous renal insufficiency ; n (%) | 632 (5.2%) | 632 (5.2%) | 499 (3.7%) | 509 (3.7%) | 1,836 (6.5%) | 1,803 (6.4%) | 2,967 (5.5%) | 2,944 (5.4%) | 0.00 |
| Glaucoma or cataracts ; n (%) | 2,530 (20.6%) | 2,514 (20.5%) | 2,365 (17.4%) | 2,305 (17.0%) | 7,914 (27.9%) | 8,032 (28.3%) | 12,809 (23.6%) | 12,851 (23.7%) | 0.00 |
| Cellulitis or abscess of toe; n (%) | 189 (1.5%) | 180 (1.5%) | 117 (0.9%) | 122 (0.9%) | 457 (1.6%) | 440 (1.6%) | 763 (1.4%) | 742 (1.4%) | 0.00 |
| Foot ulcer; n (%) | 301 (2.5%) | 290 (2.4%) | 274 (2.0%) | 296 (2.2%) | 894 (3.2%) | 912 (3.2%) | 1,469 (2.7%) | 1,498 (2.8%) | -0.01 |
| Bladder stones; n (%) | 17 (0.1%) | 8 (0.1%) | 15 (0.1%) | 14 (0.1%) | 43 (0.2%) | 41 (0.1%) | 075 (0.1%) | 063 (0.1%) | 0.00 |
| Kidney stones; n (%) | 327 (2.7%) | 308 (2.5%) | 342 (2.5%) | 334 (2.5%) | 797 (2.8%) | 799 (2.8%) | 1,466 (2.7%) | 1,441 (2.7%) | 0.00 |
| Urinary tract infections (UTIs); n (%) | 1,051 (8.6%) | 1,112 (9.1%) | 926 (6.8%) | 927 (6.8%) | 3,560 (12.6%) | 3,636 (12.8%) | 5,537 (10.2%) | 5,675 (10.5%) | -0.01 |
| Dipstick urinalysis; n (%) | 4,584 (37.4%) | 4,408 (36.0%) | 4,689 (34.5%) | 4,477 (32.9%) | 11,652 (41.1%) | 11,552 (40.8%) | 20,925 (38.6%) | 20,437 (37.7%) | 0.02 |
| Non-dipstick urinalysis; n (%) | 5,535 (45.2%) | 5,355 (43.7%) | 4,803 (35.3%) | 4,780 (35.2%) | 12,816 (45.2%) | 13,035 (46.0%) | 23,154 (42.7%) | 23,170 (42.8%) | 0.00 |
| Urine function test; n (%) | 320 (2.6%) | 272 (2.2%) | 370 (2.7%) | 340 (2.5%) | 1,106 (3.9%) | 974 (3.4%) | 1,796 (3.3%) | 1,586 (2.9%) | 0.02 |
| Cytology; n (%) | 92 (0.8%) | 84 (0.7%) | 127 (0.9%) | 113 (0.8%) | 315 (1.1%) | 286 (1.0%) | 534 (1.0%) | 483 (0.9%) | 0.01 |
| Cystos; n (%) | 175 (1.4%) | 144 (1.2%) | 193 (1.4%) | 171 (1.3%) | 491 (1.7%) | 413 (1.5%) | 859 (1.6%) | 728 (1.3%) | 0.03 |
| Other Covariates | | | | | | | | | |
| Liver disease; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 000 (0.0%) | 000 (0.0%) | #DIV/0! |
| Osteoarthritis; n (%) | 2,500 (20.4%) | 2,480 (20.2%) | 2,220 (16.3%) | 2,172 (16.0%) | 7,480 (26.4%) | 7,389 (26.1%) | 12,200 (22.5%) | 12,041 (22.2%) | 0.01 |
| Other arthritis, arthropathies and musculoskeletal pain; n (%) | 5,020 (41.0%) | 5,007 (40.9%) | 5,094 (37.5%) | 5,080 (37.4%) | 13,898 (49.0%) | 13,833 (48.8%) | 24,012 (44.3%) | 23,920 (44.1%) | 0.00 |
| Dorsopathies; n (%) | 3,323 (27.1%) | 3,268 (26.7%) | 3,062 (22.5%) | 3,026 (22.3%) | 9,051 (31.9%) | 8,893 (31.4%) | 15,436 (28.5%) | 15,187 (28.0%) | 0.01 |
| Fractures; n (%) | 348 (2.8%) | 360 (2.9%) | 347 (2.6%) | 346 (2.5%) | 1,087 (3.8%) | 1,065 (3.8%) | 1,782 (3.3%) | 1,771 (3.3%) | 0.00 |
| Falls ; n (%) | 366 (3.0%) | 366 (3.0%) | 148 (1.1%) | 137 (1.0%) | 1,009 (3.6%) | 967 (3.4%) | 1,523 (2.8%) | 1,470 (2.7%) | 0.01 |
| Osteoporosis; n (%) | 558 (4.6%) | 551 (4.5%) | 422 (3.1%) | 421 (3.1%) | 1,974 (7.0%) | 2,013 (7.1%) | 2,954 (5.5%) | 2,985 (5.5%) | 0.00 |
| Hyperthyroidism; n (%) | 126 (1.0%) | 98 (0.8%) | 103 (0.8%) | 68 (0.5%) | 339 (1.2%) | 285 (1.0%) | 568 (1.0%) | 451 (0.8%) | 0.02 |
| Hypothyroidism ; n (%) | 2,366 (19.3%) | 2,484 (20.3%) | 2,087 (15.4%) | 2,028 (14.9%) | 4,983 (17.6%) | 5,062 (17.9%) | 9,436 (17.4%) | 9,574 (17.7%) | -0.01 |
| Other disorders of thyroid gland ; n (%) | 674 (5.5%) | 663 (5.4%) | 673 (5.0%) | 689 (5.1%) | 1,711 (6.0%) | 1,749 (6.2%) | 3,058 (5.6%) | 3,101 (5.7%) | 0.00 |
| Depression; n (%) | 1,294 (10.6%) | 1,297 (10.6%) | 1,141 (8.4%) | 1,143 (8.4%) | 3,570 (12.6%) | 3,635 (12.8%) | 6,005 (11.1%) | 6,075 (11.2%) | 0.00 |
| Anxiety; n (%) | 1,173 (9.6%) | 1,157 (9.4%) | 774 (5.7%) | 753 (5.5%) | 2,518 (8.9%) | 2,547 (9.0%) | 4,465 (8.2%) | 4,457 (8.2%) | 0.00 |
| Sleep_Disorder; n (%) | 1,217 (9.9%) | 1,263 (10.3%) | 2,193 (16.1%) | 2,170 (16.0%) | 4,004 (14.1%) | 3,931 (13.9%) | 7,414 (13.7%) | 7,364 (13.6%) | 0.00 |
| Dementia; n (%) | 225 (1.8%) | 256 (2.1%) | 125 (0.9%) | 144 (1.1%) | 949 (3.3%) | 1,006 (3.6%) | 1,299 (2.4%) | 1,406 (2.6%) | -0.01 |
| Delirium; n (%) | 82 (0.7%) | 92 (0.8%) | 80 (0.6%) | 69 (0.5%) | 345 (1.2%) | 350 (1.2%) | 507 (0.9%) | 511 (0.9%) | 0.00 |
| Psychosis; n (%) | 74 (0.6%) | 80 (0.7%) | 48 (0.4%) | 52 (0.4%) | 240 (0.8%) | 256 (0.9%) | 362 (0.7%) | 388 (0.7%) | 0.00 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|---------------|---------------|---------------|---------------|----------------|----------------|----------------|----------------|---------|
| Obesity; n (%) | 4,171 (34.0%) | 4,169 (34.0%) | 3,000 (22.1%) | 2,988 (22.0%) | 7,848 (27.7%) | 7,815 (27.6%) | 15,019 (27.7%) | 14,972 (27.6%) | 0.00 |
| Overweight; n (%) | 509 (4.2%) | 525 (4.3%) | 281 (2.1%) | 264 (1.9%) | 804 (2.8%) | 818 (2.9%) | 1,594 (2.9%) | 1,607 (3.0%) | -0.01 |
| Smoking; n (%) | 1,387 (11.3%) | 1,375 (11.2%) | 650 (4.8%) | 629 (4.6%) | 3,607 (12.7%) | 3,542 (12.5%) | 5,644 (10.4%) | 5,546 (10.2%) | 0.01 |
| Alcohol abuse or dependence; n (%) | 41 (0.3%) | 46 (0.4%) | 24 (0.2%) | 37 (0.3%) | 105 (0.4%) | 97 (0.3%) | 170 (0.3%) | 180 (0.3%) | 0.00 |
| Drug abuse or dependence; n (%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 000 (0.0%) | 000 (0.0%) | #DIV/0! |
| COPD; n (%) | 1,011 (8.3%) | 1,025 (8.4%) | 652 (4.8%) | 655 (4.8%) | 3,311 (11.7%) | 3,256 (11.5%) | 4,974 (9.2%) | 4,936 (9.1%) | 0.00 |
| Asthma; n (%) | 915 (7.5%) | 900 (7.3%) | 800 (5.9%) | 801 (5.9%) | 2,455 (8.7%) | 2,417 (8.5%) | 4,170 (7.7%) | 4,118 (7.6%) | 0.00 |
| Obstructive sleep apnea; n (%) | 2,161 (17.6%) | 2,192 (17.9%) | 2,342 (17.2%) | 2,318 (17.1%) | 4,225 (14.9%) | 4,227 (14.9%) | 8,728 (16.1%) | 8,737 (16.1%) | 0.00 |
| Pneumonia; n (%) | 219 (1.8%) | 249 (2.0%) | 265 (1.9%) | 241 (1.8%) | 763 (2.7%) | 788 (2.8%) | 1,247 (2.3%) | 1,278 (2.4%) | -0.01 |
| Imaging; n (%) | 8 (0.1%) | 15 (0.1%) | 8 (0.1%) | 10 (0.1%) | 37 (0.1%) | 34 (0.1%) | 53 (0.1%) | 59 (0.1%) | 0.00 |
| Diabetes Medications | | | | | | | | | |
| DM Medications - AGIs; n (%) | 36 (0.3%) | 40 (0.3%) | 51 (0.4%) | 48 (0.4%) | 114 (0.4%) | 120 (0.4%) | 201 (0.4%) | 208 (0.4%) | 0.00 |
| DM Medications - Glitazones; n (%) | 1,225 (10.0%) | 1,202 (9.8%) | 1,799 (13.2%) | 1,801 (13.3%) | 2,672 (9.4%) | 2,555 (9.0%) | 5,696 (10.5%) | 5,558 (10.3%) | 0.01 |
| DM Medications - Insulin; n (%) | 2,389 (19.5%) | 2,476 (20.2%) | 2,319 (17.1%) | 2,561 (18.8%) | 6,609 (23.3%) | 6,878 (24.3%) | 11,317 (20.9%) | 11,915 (22.0%) | -0.03 |
| DM Medications - Meglitinides; n (%) | 133 (1.1%) | 144 (1.2%) | 295 (2.2%) | 297 (2.2%) | 570 (2.0%) | 585 (2.1%) | 998 (1.8%) | 1,026 (1.9%) | -0.01 |
| DM Medications - Metformin; n (%) | 7,287 (59.5%) | 7,222 (58.9%) | 8,603 (63.3%) | 8,476 (62.4%) | 17,200 (60.7%) | 17,179 (60.6%) | 33,090 (61.1%) | 32,877 (60.7%) | 0.01 |
| Concomitant initiation or current use of SGLT2i; n (%) | 638 (5.2%) | 670 (5.5%) | 681 (5.0%) | 681 (5.0%) | 1,135 (4.0%) | 1,182 (4.2%) | 2,454 (4.5%) | 2,533 (4.7%) | -0.01 |
| Concomitant initiation or current use of AGIs; n (%) | 25 (0.2%) | 22 (0.2%) | 43 (0.3%) | 29 (0.2%) | 70 (0.2%) | 82 (0.3%) | 138 (0.3%) | 133 (0.2%) | 0.02 |
| Concomitant initiation or current use of Glitazones; n (%) | 916 (7.5%) | 864 (7.1%) | 1,260 (9.3%) | 1,289 (9.5%) | 2,006 (7.1%) | 1,949 (6.9%) | 4,182 (7.7%) | 4,102 (7.6%) | 0.00 |
| Concomitant initiation or current use of DPP4i; n (%) | 109 (0.9%) | 109 (0.9%) | 130 (1.0%) | 124 (0.9%) | 217 (0.8%) | 225 (0.8%) | 456 (0.8%) | 458 (0.8%) | 0.00 |
| Concomitant initiation or current use of Insulin; n (%) | 1,423 (11.6%) | 1,523 (12.4%) | 1,389 (10.2%) | 1,588 (11.7%) | 4,047 (14.3%) | 4,309 (15.2%) | 6,859 (12.7%) | 7,420 (13.7%) | -0.03 |
| Concomitant initiation or current use of Meglitinides; n (%) | 72 (0.6%) | 84 (0.7%) | 170 (1.3%) | 207 (1.5%) | 392 (1.4%) | 398 (1.4%) | 634 (1.2%) | 689 (1.3%) | -0.01 |
| Concomitant initiation or current use of Metformin; n (%) | 5,832 (47.6%) | 5,784 (47.2%) | 6,814 (50.1%) | 6,740 (49.6%) | 13,754 (48.5%) | 13,814 (48.7%) | 26,400 (48.7%) | 26,338 (48.6%) | 0.00 |
| Past use of SGLT2i ; n (%) | 264 (2.2%) | 278 (2.3%) | 242 (1.8%) | 236 (1.7%) | 526 (1.9%) | 530 (1.9%) | 1,032 (1.9%) | 1,044 (1.9%) | 0.00 |
| Past use of AGIs ; n (%) | 11 (0.1%) | 18 (0.1%) | 8 (0.1%) | 19 (0.1%) | 44 (0.2%) | 38 (0.1%) | 063 (0.1%) | 075 (0.1%) | 0.00 |
| Past use of Glitazones ; n (%) | 309 (2.5%) | 338 (2.8%) | 539 (4.0%) | 512 (3.8%) | 666 (2.4%) | 606 (2.1%) | 1,514 (2.8%) | 1,456 (2.7%) | 0.01 |
| Past use of DPP4i ; n (%) | 476 (3.9%) | 463 (3.8%) | 782 (5.8%) | 738 (5.4%) | 1,389 (4.9%) | 1,313 (4.6%) | 2,647 (4.9%) | 2,514 (4.6%) | 0.01 |
| Past use of Insulin ; n (%) | 966 (7.9%) | 953 (7.8%) | 930 (6.8%) | 973 (7.2%) | 2,565 (9.1%) | 2,569 (9.1%) | 4,461 (8.2%) | 4,495 (8.3%) | 0.00 |
| Past use of Meglitinides ; n (%) | 61 (0.5%) | 60 (0.5%) | 125 (0.9%) | 90 (0.7%) | 178 (0.6%) | 187 (0.7%) | 364 (0.7%) | 337 (0.6%) | 0.01 |
| Past use of metformin (final) ; n (%) | 1,455 (11.9%) | 1,438 (11.7%) | 1,789 (13.2%) | 1,736 (12.8%) | 3,446 (12.2%) | 3,365 (11.9%) | 6,690 (12.3%) | 6,539 (12.1%) | 0.01 |
| Other Medications | | | | | | | | | |
| Use of ACE inhibitors; n (%) | 5,063 (41.3%) | 5,097 (41.6%) | 5,527 (40.7%) | 5,554 (40.9%) | 11,457 (40.4%) | 11,611 (41.0%) | 22,047 (40.7%) | 22,262 (41.1%) | -0.01 |
| Use of ARBs; n (%) | 4,202 (34.3%) | 4,160 (34.0%) | 5,158 (38.0%) | 5,036 (37.1%) | 10,227 (36.1%) | 10,180 (35.9%) | 19,587 (36.2%) | 19,376 (35.8%) | 0.01 |
| Use of Loop Diuretics; n (%) | 2,037 (16.6%) | 2,076 (16.9%) | 2,059 (15.1%) | 2,080 (15.3%) | 6,079 (21.5%) | 6,171 (21.8%) | 10,175 (18.8%) | 10,327 (19.1%) | -0.01 |
| Use of other diuretics; n (%) | 501 (4.1%) | 516 (4.2%) | 565 (4.2%) | 591 (4.3%) | 1,463 (5.2%) | 1,427 (5.0%) | 2,529 (4.7%) | 2,534 (4.7%) | 0.00 |
| Use of nitrates-United; n (%) | 852 (7.0%) | 864 (7.1%) | 907 (6.7%) | 968 (7.1%) | 2,172 (7.7%) | 2,226 (7.9%) | 3,931 (7.3%) | 4,058 (7.5%) | -0.01 |
| Use of other hypertension drugs; n (%) | 871 (7.1%) | 875 (7.1%) | 900 (6.6%) | 899 (6.6%) | 2,265 (8.0%) | 2,241 (7.9%) | 4,036 (7.4%) | 4,015 (7.4%) | 0.00 |
| Use of digoxin; n (%) | 176 (1.4%) | 173 (1.4%) | 182 (1.3%) | 221 (1.6%) | 623 (2.2%) | 600 (2.1%) | 981 (1.8%) | 994 (1.8%) | 0.00 |
| Use of Anti-arrhythmics; n (%) | 207 (1.7%) | 203 (1.7%) | 222 (1.6%) | 224 (1.6%) | 668 (2.4%) | 636 (2.2%) | 1,097 (2.0%) | 1,063 (2.0%) | 0.00 |
| Use of COPD/asthma meds; n (%) | 2,039 (16.6%) | 2,073 (16.9%) | 2,388 (17.6%) | 2,380 (17.5%) | 5,744 (20.3%) | 5,694 (20.1%) | 10,171 (18.8%) | 10,147 (18.7%) | 0.00 |
| Use of statins; n (%) | 8,485 (69.2%) | 8,487 (69.3%) | 9,378 (69.0%) | 9,460 (69.6%) | 20,077 (70.8%) | 20,155 (71.1%) | 37,940 (70.0%) | 38,102 (70.3%) | -0.01 |
| Use of other lipid-lowering drugs; n (%) | 1,675 (13.7%) | 1,649 (13.5%) | 2,457 (18.1%) | 2,425 (17.8%) | 4,125 (14.6%) | 4,179 (14.7%) | 8,257 (15.2%) | 8,253 (15.2%) | 0.00 |
| Use of antiplatelet agents; n (%) | 1,783 (14.6%) | 1,827 (14.9%) | 2,483 (18.3%) | 2,532 (18.6%) | 4,427 (15.6%) | 4,465 (15.8%) | 8,693 (16.0%) | 8,824 (16.3%) | -0.01 |
| Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%) | 911 (7.4%) | 886 (7.2%) | 847 (6.2%) | 849 (6.2%) | 2,747 (9.7%) | 2,722 (9.6%) | 4,505 (8.3%) | 4,457 (8.2%) | 0.00 |
| Use of heparin and other low-molecular weight heparins; n (%) | 60 (0.5%) | 67 (0.5%) | 0 (0.0%) | 0 (0.0%) | 153 (0.5%) | 140 (0.5%) | 213 (0.4%) | 207 (0.4%) | 0.00 |
| Use of NSAIDs; n (%) | 2,128 (17.4%) | 2,143 (17.5%) | 2,463 (18.1%) | 2,389 (17.6%) | 5,307 (18.7%) | 5,160 (18.2%) | 9,898 (18.3%) | 9,692 (17.9%) | 0.01 |
| Use of oral corticosteroids; n (%) | 2,113 (17.2%) | 2,056 (16.8%) | 2,208 (16.2%) | 2,148 (15.8%) | 5,336 (18.8%) | 5,278 (18.6%) | 9,657 (17.8%) | 9,482 (17.5%) | 0.01 |
| Use of bisphosphonate (United); n (%) | 247 (2.0%) | 244 (2.0%) | 223 (1.6%) | 210 (1.5%) | 674 (2.4%) | 727 (2.6%) | 1,144 (2.1%) | 1,181 (2.2%) | -0.01 |
| Use of opioids; n (%) | 3,459 (28.2%) | 3,463 (28.3%) | 3,962 (29.2%) | 3,881 (28.6%) | 8,527 (30.1%) | 8,497 (30.0%) | 15,948 (29.4%) | 15,841 (29.2%) | 0.00 |
| Use of antidepressants; n (%) | 3,896 (31.8%) | 3,877 (31.6%) | 4,178 (30.7%) | 4,117 (30.3%) | 9,729 (34.3%) | 9,631 (34.0%) | 17,803 (32.9%) | 17,625 (32.5%) | 0.01 |
| Use of antipsychotics; n (%) | 298 (2.4%) | 291 (2.4%) | 259 (1.9%) | 251 (1.8%) | 740 (2.6%) | 738 (2.6%) | 1,297 (2.4%) | 1,280 (2.4%) | 0.00 |
| Use of anticonvulsants; n (%) | 2,473 (20.2%) | 2,503 (20.4%) | 2,053 (15.1%) | 2,005 (14.8%) | 5,861 (20.7%) | 5,797 (20.5%) | 10,387 (19.2%) | 10,305 (19.0%) | 0.01 |
| Use of lithium; n (%) | 20 (0.2%) | 11 (0.1%) | 37 (0.3%) | 15 (0.1%) | 48 (0.2%) | 38 (0.1%) | 105 (0.2%) | 064 (0.1%) | 0.03 |
| Use of Benzos; n (%) | 1,479 (12.1%) | 1,453 (11.9%) | 1,788 (13.2%) | 1,768 (13.0%) | 3,457 (12.2%) | 3,377 (11.9%) | 6,724 (12.4%) | 6,598 (12.2%) | 0.01 |
| Use of anxiolytics/hypnotics; n (%) | 923 (7.5%) | 931 (7.6%) | 1,214 (8.9%) | 1,203 (8.9%) | 2,382 (8.4%) | 2,284 (8.1%) | 4,519 (8.3%) | 4,418 (8.2%) | 0.00 |
| Use of dementia meds; n (%) | 117 (1.0%) | 120 (1.0%) | 91 (0.7%) | 98 (0.7%) | 587 (2.1%) | 614 (2.2%) | 795 (1.5%) | 832 (1.5%) | 0.00 |
| Use of antiparkinsonian meds; n (%) | 465 (3.8%) | 423 (3.5%) | 439 (3.2%) | 428 (3.1%) | 1,225 (4.3%) | 1,242 (4.4%) | 2,129 (3.9%) | 2,093 (3.9%) | 0.00 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|-----------------------|-----------------------|----------------------|-----------------------|---------------|--------------|------------------|------------------|---------|
| Any use of pramlintide; n (%) | 0 (0.0%) | 5 (0.0%) | 4 (0.0%) | 21 (0.2%) | 1 (0.0%) | 16 (0.1%) | 005 (0.0%) | 042 (0.1%) | -0.04 |
| Any use of 1st generation sulfonylureas; n (%) | 1 (0.0%) | 0 (0.0%) | 8 (0.1%) | 1 (0.0%) | 12 (0.0%) | 3 (0.0%) | 021 (0.0%) | 004 (0.0%) | 0.00 |
| Entresto (sacubitril/valsartan); n (%) | 28 (0.2%) | 36 (0.3%) | 10 (0.1%) | 9 (0.1%) | 22 (0.1%) | 26 (0.1%) | 060 (0.1%) | 071 (0.1%) | 0.00 |
| Initiation as monotherapy ; n (%) | 1,596 (13.0%) | 1,798 (14.7%) | 1,351 (9.9%) | 1,557 (11.5%) | 2,855 (10.1%) | 2,775 (9.8%) | 5,802 (10.7%) | 6,130 (11.3%) | -0.02 |
| Labs | | | | | | | 25,844 | 25,844 | |
| Lab values- HbA1c (%) ; n (%) | 4,749 (38.8%) | 4,611 (37.6%) | 981 (7.2%) | 738 (5.4%) | N/A | N/A | 5,730 (22.2%) | 5,349 (20.7%) | 0.04 |
| Lab values- HbA1c (%) (within 3 months); n (%) | 3,629 (29.6%) | 3,522 (28.7%) | 743 (5.5%) | 580 (4.3%) | N/A | N/A | 4,372 (16.9%) | 4,102 (15.9%) | 0.03 |
| Lab values- HbA1c (%) (within 6 months); n (%) | 4,749 (38.8%) | 4,611 (37.6%) | 981 (7.2%) | 738 (5.4%) | N/A | N/A | 5,730 (22.2%) | 5,349 (20.7%) | 0.04 |
| Lab values- BNP; n (%) | 121 (1.0%) | 124 (1.0%) | 21 (0.2%) | 23 (0.2%) | N/A | N/A | 142 (0.5%) | 147 (0.6%) | -0.01 |
| Lab values- BNP (within 3 months); n (%) | 72 (0.6%) | 81 (0.7%) | 12 (0.1%) | 21 (0.2%) | N/A | N/A | 084 (0.3%) | 102 (0.4%) | -0.02 |
| Lab values- BNP (within 6 months); n (%) | 121 (1.0%) | 124 (1.0%) | 21 (0.2%) | 23 (0.2%) | N/A | N/A | 142 (0.5%) | 147 (0.6%) | -0.01 |
| Lab values- BUN (mg/dl); n (%) | 4,869 (39.7%) | 4,746 (38.7%) | 902 (6.6%) | 766 (5.6%) | N/A | N/A | 5,771 (22.3%) | 5,512 (21.3%) | 0.02 |
| Lab values- BUN (mg/dl) (within 3 months); n (%) | 3,694 (30.1%) | 3,594 (29.3%) | 654 (4.8%) | 581 (4.3%) | N/A | N/A | 4,348 (16.8%) | 4,175 (16.2%) | 0.02 |
| Lab values- BUN (mg/dl) (within 6 months); n (%) | 4,869 (39.7%) | 4,746 (38.7%) | 902 (6.6%) | 766 (5.6%) | N/A | N/A | 5,771 (22.3%) | 5,512 (21.3%) | 0.02 |
| Lab values- Creatinine (mg/dl) ; n (%) | 4,980 (40.6%) | 4,900 (40.0%) | 955 (7.0%) | 797 (5.9%) | N/A | N/A | 5,935 (23.0%) | 5,697 (22.0%) | 0.02 |
| Lab values- Creatinine (mg/dl) (within 3 months); n (%) | 3,790 (30.9%) | 3,714 (30.3%) | 695 (5.1%) | 605 (4.5%) | N/A | N/A | 4,485 (17.4%) | 4,319 (16.7%) | 0.02 |
| Lab values- Creatinine (mg/dl) (within 6 months); n (%) | 4,980 (40.6%) | 4,900 (40.0%) | 955 (7.0%) | 797 (5.9%) | N/A | N/A | 5,935 (23.0%) | 5,697 (22.0%) | 0.02 |
| Lab values- HDL level (mg/dl); n (%) | 4,142 (33.8%) | 3,943 (32.2%) | 903 (6.6%) | 681 (5.0%) | N/A | N/A | 5,045 (19.5%) | 4,624 (17.9%) | 0.04 |
| Lab values- HDL level (mg/dl) (within 3 months); n (%) | 2,951 (24.1%) | 2,818 (23.0%) | 630 (4.6%) | 508 (3.7%) | N/A | N/A | 3,581 (13.9%) | 3,326 (12.9%) | 0.03 |
| Lab values- HDL level (mg/dl) (within 6 months); n (%) | 4,142 (33.8%) | 3,943 (32.2%) | 903 (6.6%) | 681 (5.0%) | N/A | N/A | 5,045 (19.5%) | 4,624 (17.9%) | 0.04 |
| Lab values- LDL level (mg/dl) ; n (%) | 4,233 (34.5%) | 4,065 (33.2%) | 932 (6.9%) | 704 (5.2%) | N/A | N/A | 5,165 (20.0%) | 4,769 (18.5%) | 0.04 |
| Lab values- LDL level (mg/dl) (within 3 months); n (%) | 3,015 (24.6%) | 2,914 (23.8%) | 648 (4.8%) | 520 (3.8%) | N/A | N/A | 3,663 (14.2%) | 3,434 (13.3%) | 0.03 |
| Lab values- LDL level (mg/dl) (within 6 months); n (%) | 4,233 (34.5%) | 4,065 (33.2%) | 932 (6.9%) | 704 (5.2%) | N/A | N/A | 5,165 (20.0%) | 4,769 (18.5%) | 0.04 |
| Lab values- NT-proBNP; n (%) | 10 (0.1%) | 30 (0.2%) | 1 (0.0%) | 3 (0.0%) | N/A | N/A | 11 (0.0%) | 0 (0.1%) | - |
| Lab values- NT-proBNP (within 3 months); n (%) | 5 (0.0%) | 20 (0.2%) | 0 (0.0%) | 1 (0.0%) | N/A | N/A | 05 (0.0%) | 0 (0.1%) | - |
| Lab values- NT-proBNP (within 6 months); n (%) | 10 (0.1%) | 30 (0.2%) | 1 (0.0%) | 3 (0.0%) | N/A | N/A | 11 (0.0%) | 33 (0.1%) | - |
| Lab values- Total cholesterol (mg/dl) ; n (%) | 4,202 (34.3%) | 4,042 (33.0%) | 911 (6.7%) | 691 (5.1%) | N/A | N/A | 5,113 (19.8%) | 4,733 (18.3%) | 0.04 |
| Lab values- Total cholesterol (mg/dl) (within 3 months); n (%) | 3,000 (24.5%) | 2,889 (23.6%) | 634 (4.7%) | 517 (3.8%) | N/A | N/A | 3,634 (14.1%) | 3,406 (13.2%) | 0.03 |
| Lab values- Total cholesterol (mg/dl) (within 6 months); n (%) | 4,202 (34.3%) | 4,042 (33.0%) | 911 (6.7%) | 691 (5.1%) | N/A | N/A | 5,113 (19.8%) | 4,733 (18.3%) | 0.04 |
| Lab values- Triglyceride level (mg/dl); n (%) | 4,168 (34.0%) | 3,999 (32.6%) | 901 (6.6%) | 676 (5.0%) | N/A | N/A | 5,069 (19.6%) | 4,675 (18.1%) | 0.04 |
| Lab values- Triglyceride level (mg/dl) (within 3 months); n (%) | 2,979 (24.3%) | 2,862 (23.4%) | 629 (4.6%) | 503 (3.7%) | N/A | N/A | 3,608 (14.0%) | 3,365 (13.0%) | 0.03 |
| Lab values- Triglyceride level (mg/dl) (within 6 months); n (%) | 4,168 (34.0%) | 3,999 (32.6%) | 901 (6.6%) | 676 (5.0%) | N/A | N/A | 5,069 (19.6%) | 4,675 (18.1%) | 0.04 |
| Lab result number- HbA1c (%) mean (only 2 to 20 included) | 4,726 | 4,589 | 877 | 694 | N/A | N/A | 5,603 | 5,283 | |
| ...mean (sd) | 8.09 (1.82) | 7.86 (1.75) | 8.13 (1.91) | 7.85 (1.83) | N/A | N/A | 8.10 (1.83) | 7.86 (1.76) | 0.13 |
| ...median [IQR] | 7.70 [6.90, 8.85] | 7.40 [6.60, 8.70] | 7.60 [6.90, 8.90] | 7.40 [6.50, 8.76] | N/A | N/A | 7.68 (1.83) | 7.40 (1.76) | 0.16 |
| ...Missing; n (%) | 7,527 (61.4%) | 7,664 (62.5%) | 12,714 (93.5%) | 12,897 (94.9%) | N/A | N/A | 20,241 (78.3%) | 20,561 (79.6%) | -0.03 |
| Lab result number- BNP mean | 121 | 124 | 21 | 23 | N/A | N/A | 142 | 147 | |
| ...mean (sd) | 146.97 (207.33) | 105.07 (131.54) | 72.61 (105.14) | 105.16 (203.02) | N/A | N/A | 135.97 (196.72) | 105.08 (145.18) | 0.18 |
| ...median [IQR] | 67.00 [20.55, 178.80] | 46.65 [21.92, 138.88] | 42.00 [10.50, 64.50] | 24.00 [14.00, 124.00] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 12,132 (99.0%) | 12,129 (99.0%) | 13,570 (99.8%) | 13,568 (99.8%) | N/A | N/A | 25,702 (99.5%) | 25,697 (99.4%) | 0.01 |
| Lab result number- BUN (mg/dl) mean | 4,869 | 4,746 | 902 | 766 | N/A | N/A | 5,771 | 5,512 | |
| ...mean (sd) | 18.85 (8.25) | 18.98 (7.61) | 556.53 (9,565.83) | 697.32 (11,098.36) | N/A | N/A | 102.89 (3780.71) | 113.25 (4135.75) | 0.00 |
| ...median [IQR] | 17.00 [13.63, 22.00] | 17.50 [14.00, 22.00] | 17.00 [14.00, 22.00] | 17.00 [14.00, 22.00] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 7,384 (60.3%) | 7,507 (61.3%) | 12,689 (93.4%) | 12,825 (94.4%) | N/A | N/A | 20,073 (77.7%) | 20,332 (78.7%) | -0.02 |
| Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included) | 4,951 | 4,872 | 855 | 730 | N/A | N/A | 5,806 | 5,602 | |
| ...mean (sd) | 1.04 (0.41) | 1.02 (0.36) | 1.03 (0.38) | 0.99 (0.30) | N/A | N/A | 1.04 (0.41) | 1.02 (0.35) | 0.05 |
| ...median [IQR] | 0.94 [0.79, 1.17] | 0.95 [0.78, 1.16] | 0.97 [0.80, 1.15] | 0.93 [0.78, 1.13] | N/A | N/A | 0.94 (0.41) | 0.95 (0.35) | -0.03 |
| ...Missing; n (%) | 7,302 (59.6%) | 7,381 (60.2%) | 12,736 (93.7%) | 12,861 (94.6%) | N/A | N/A | 20,038 (77.5%) | 20,242 (78.3%) | -0.02 |
| Lab result number- HDL level (mg/dl) mean (only <=5000 included) | 4,142 | 3,943 | 901 | 679 | N/A | N/A | 5,043 | 4,622 | |
| ...mean (sd) | 46.63 (13.79) | 46.80 (13.34) | 45.37 (14.04) | 44.85 (14.28) | N/A | N/A | 46.40 (13.84) | 46.51 (13.48) | -0.01 |
| ...median [IQR] | 44.50 [37.00, 54.00] | 45.00 [37.50, 54.00] | 44.00 [36.50, 53.00] | 43.50 [36.00, 53.00] | N/A | N/A | 44.41 (13.84) | 44.78 (13.48) | -0.03 |
| ...Missing; n (%) | 8,111 (66.2%) | 8,310 (67.8%) | 12,690 (93.4%) | 12,912 (95.0%) | N/A | N/A | 20,801 (80.5%) | 21,222 (82.1%) | -0.04 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|---|-------------------------|-------------------------|-------------------------|-------------------------|-------------------|-------------------|---------------------|-----------------|---------|
| Lab result number- LDL level (mg/dl) mean (only <=5000 included) | 4,143 | 3,983 | 870 | 619 | N/A | N/A | 5,013 | 4,602 | |
| ...mean (sd) | 87.05 (39.40) | 83.22 (37.92) | 92.02 (41.04) | 83.66 (41.01) | N/A | N/A | 87.91 (39.69) | 83.28 (38.35) | 0.12 |
| ...median [IQR] | 84.00 [63.00, 109.00] | 79.50 [61.00, 103.33] | 88.25 [67.00, 115.50] | 83.00 [62.00, 107.00] | N/A | N/A | 84.74 (39.69) | 79.97 (38.35) | 0.12 |
| ...Missing; n (%) | 8,110 (66.2%) | 8,270 (67.5%) | 12,721 (93.6%) | 12,972 (95.4%) | N/A | N/A | 20,831 (80.6%) | 21,242 (82.2%) | -0.04 |
| Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included) | 4,198 | 4,041 | 909 | 688 | N/A | N/A | 5,107 | 4,729 | |
| ...mean (sd) | 174.87 (45.66) | 168.95 (44.31) | 177.69 (50.94) | 171.56 (49.44) | N/A | N/A | 175.37 (46.65) | 169.33 (45.10) | 0.13 |
| ...median [IQR] | 169.00 [144.00, 199.00] | 162.50 [140.00, 192.00] | 173.00 [146.25, 204.00] | 166.25 [143.00, 198.00] | N/A | N/A | 169.71 (46.65) | 163.05 (45.10) | 0.15 |
| ...Missing; n (%) | 8,055 (65.7%) | 8,212 (67.0%) | 12,682 (93.3%) | 12,903 (94.9%) | N/A | N/A | 20,737 (80.2%) | 21,115 (81.7%) | -0.04 |
| Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included) | 4,168 | 3,999 | 899 | 674 | N/A | N/A | 5,067 | 4,673 | |
| ...mean (sd) | 189.65 (149.17) | 179.99 (140.90) | 191.74 (149.61) | 186.92 (137.38) | N/A | N/A | 190.02 (149.26) | 180.99 (140.41) | 0.06 |
| ...median [IQR] | 155.00 [109.50, 223.00] | 150.00 [107.00, 212.00] | 157.00 [108.00, 220.50] | 152.00 [108.00, 224.00] | N/A | N/A | 155.35 (149.26) | 150.29 (140.41) | 0.03 |
| ...Missing; n (%) | 8,085 (66.0%) | 8,254 (67.4%) | 12,692 (93.4%) | 12,917 (95.0%) | N/A | N/A | 20,777 (80.4%) | 21,171 (81.9%) | -0.04 |
| Lab result number- Hemoglobin mean (only >0 included) | 3,487 | 3,344 | 640 | 521 | N/A | N/A | 4,127 | 3,865 | |
| ...mean (sd) | 13.46 (1.66) | 13.48 (1.58) | 16,304.65 (395,377.51) | 308.91 (6,746.28) | N/A | N/A | 2539.84 (155633.49) | 53.30 (2475.48) | 0.02 |
| ...median [IQR] | 13.50 [12.40, 14.50] | 13.50 [12.40, 14.50] | 13.50 [12.40, 14.60] | 13.50 [12.50, 14.65] | N/A | N/A | #VALUE! | #VALUE! | #VALUE! |
| ...Missing; n (%) | 8,766 (71.5%) | 8,909 (72.7%) | 12,951 (95.3%) | 13,070 (96.2%) | N/A | N/A | 21,717 (84.0%) | 21,979 (85.0%) | -0.03 |
| Lab result number- Serum sodium mean (only >90 and < 190 included) | 4,853 | 4,782 | 895 | 717 | N/A | N/A | 5,748 | 5,499 | |
| ...mean (sd) | 139.54 (2.72) | 139.80 (2.62) | 139.15 (2.58) | 139.15 (2.51) | N/A | N/A | 139.48 (2.70) | 139.72 (2.61) | -0.09 |
| ...median [IQR] | 140.00 [138.00, 141.00] | 140.00 [138.00, 141.50] | 139.00 [137.50, 141.00] | 139.00 [137.88, 141.00] | N/A | N/A | 139.84 (2.70) | 139.87 (2.61) | -0.01 |
| ...Missing; n (%) | 7,400 (60.4%) | 7,471 (61.0%) | 12,696 (93.4%) | 12,874 (94.7%) | N/A | N/A | 20,096 (77.8%) | 20,345 (78.7%) | -0.02 |
| Lab result number- Albumin mean (only >0 and <=10 included) | 4,530 | 4,437 | 788 | 676 | N/A | N/A | 5,318 | 5,113 | |
| ...mean (sd) | 4.23 (0.32) | 4.22 (0.30) | 4.15 (0.58) | 4.11 (0.62) | N/A | N/A | 4.22 (0.37) | 4.21 (0.36) | 0.03 |
| ...median [IQR] | 4.25 [4.05, 4.43] | 4.20 [4.00, 4.40] | 4.20 [4.00, 4.40] | 4.20 [4.00, 4.40] | N/A | N/A | 4.24 (0.37) | 4.20 (0.36) | 0.11 |
| ...Missing; n (%) | 7,723 (63.0%) | 7,816 (63.8%) | 12,803 (94.2%) | 12,915 (95.0%) | N/A | N/A | 20,526 (79.4%) | 20,731 (80.2%) | -0.02 |
| Lab result number- Glucose (fasting or random) mean (only 10-1000 included) | 4,843 | 4,782 | 885 | 704 | N/A | N/A | 5,728 | 5,486 | |
| ...mean (sd) | 169.27 (69.50) | 160.44 (68.75) | 169.76 (71.09) | 164.21 (69.10) | N/A | N/A | 169.35 (69.75) | 160.92 (68.80) | 0.12 |
| ...median [IQR] | 152.00 [123.00, 197.00] | 143.00 [113.00, 186.00] | 152.00 [122.00, 195.75] | 145.25 [115.00, 192.25] | N/A | N/A | 152.00 (69.75) | 143.29 (68.80) | 0.13 |
| ...Missing; n (%) | 7,410 (60.5%) | 7,471 (61.0%) | 12,706 (93.5%) | 12,887 (94.8%) | N/A | N/A | 20,116 (77.8%) | 20,358 (78.8%) | -0.02 |
| Lab result number- Potassium mean (only 1-7 included) | 4,941 | 4,865 | 883 | 749 | N/A | N/A | 5,824 | 5,614 | |
| ...mean (sd) | 4.44 (0.43) | 4.44 (0.42) | 4.34 (0.44) | 4.33 (0.46) | N/A | N/A | 4.42 (0.43) | 4.43 (0.43) | -0.02 |
| ...median [IQR] | 4.41 [4.20, 4.70] | 4.40 [4.20, 4.70] | 4.30 [4.00, 4.70] | 4.30 [4.00, 4.60] | N/A | N/A | 4.39 (0.43) | 4.39 (0.43) | 0.00 |
| ...Missing; n (%) | 7,312 (59.7%) | 7,388 (60.3%) | 12,708 (93.5%) | 12,842 (94.5%) | N/A | N/A | 20,020 (77.5%) | 20,230 (78.3%) | -0.02 |
| Comorbidity Scores | | | | | | | | | |
| CCI (180 days)- ICD9 and ICD10 | | | | | | | | | |
| ...mean (sd) | 2.71 (1.81) | 2.75 (1.84) | 2.04 (1.47) | 2.05 (1.50) | 2.89 (2.02) | 2.91 (2.02) | 2.64 (1.85) | 2.66 (1.86) | -0.01 |
| ...median [IQR] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 2.00 [1.00, 3.00] | 2.00 [1.00, 3.00] | 2.00 [1.00, 4.00] | 2.00 [1.00, 4.00] | 2.00 (1.85) | 2.00 (1.86) | 0.00 |
| Frailty Score: Qualitative Version 365 days as Categories, | | | | | | | | | |
| ...0; n (%) | 6,556 (53.5%) | 6,470 (52.8%) | 4,392 (32.3%) | 4,325 (31.8%) | 9,934 (35.1%) | 9,809 (34.6%) | 20,882 (38.5%) | 20,604 (38.0%) | 0.01 |
| ...1 to 2; n (%) | 3,663 (29.9%) | 3,793 (31.0%) | 5,956 (43.8%) | 6,111 (45.0%) | 9,080 (32.0%) | 9,317 (32.9%) | 18,699 (34.5%) | 19,221 (35.5%) | -0.02 |
| ...3 or more; n (%) | 2,034 (16.6%) | 1,990 (16.2%) | 3,243 (23.9%) | 3,155 (23.2%) | 9,324 (32.9%) | 9,212 (32.5%) | 14,601 (26.9%) | 14,357 (26.5%) | 0.01 |
| Frailty Score: Empirical Version 365 days as Categories, | | | | | | | | | |
| ...< 0.12908; n (%) | 2,200 (18.0%) | 2,163 (17.7%) | 2,347 (17.3%) | 2,284 (16.8%) | 2,788 (9.8%) | 2,572 (9.1%) | 7,335 (13.5%) | 7,019 (13.0%) | 0.01 |
| ...0.12908 - 0.1631167; n (%) | 4,002 (32.7%) | 3,922 (32.0%) | 4,497 (33.1%) | 4,507 (33.2%) | 6,595 (23.3%) | 6,757 (23.8%) | 15,094 (27.9%) | 15,186 (28.0%) | 0.00 |
| ...> 0.1631167; n (%) | 6,051 (49.4%) | 6,168 (50.3%) | 6,747 (49.6%) | 6,800 (50.0%) | 18,955 (66.9%) | 19,009 (67.1%) | 31,753 (58.6%) | 31,977 (59.0%) | -0.01 |
| Non-Frailty; n (%) | 7,239 (59.1%) | 7,551 (61.6%) | 7,578 (55.8%) | 7,639 (56.2%) | 1,368 (4.8%) | 1,168 (4.1%) | 16,185 (29.9%) | 16,358 (30.2%) | -0.01 |
| Frailty Score (mean): Qualitative Version 365 days, | | | | | | | | | |
| ...mean (sd) | 1.15 (1.76) | 1.11 (1.65) | 1.60 (1.71) | 1.58 (1.64) | 1.99 (2.24) | 1.97 (2.22) | 1.70 (2.01) | 1.68 (1.97) | 0.01 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 1.00 [0.00, 3.00] | 1.00 [0.00, 3.00] | 0.77 (2.01) | 0.77 (1.97) | 0.00 |
| Frailty Score (mean): Empirical Version 365 days, | | | | | | | | | |
| ...mean (sd) | 0.17 (0.05) | 0.17 (0.05) | 0.16 (0.05) | 0.16 (0.05) | 0.20 (0.06) | 0.20 (0.07) | 0.18 (0.06) | 0.18 (0.06) | 0.00 |
| ...median [IQR] | 0.16 [0.14, 0.20] | 0.16 [0.14, 0.20] | 0.16 [0.13, 0.19] | 0.16 [0.13, 0.19] | 0.19 [0.15, 0.23] | 0.18 [0.15, 0.23] | 0.18 (0.06) | 0.17 (0.06) | 0.17 |
| Healthcare Utilization | | | | | | | | | |
| Any hospitalization; n (%) | 941 (7.7%) | 916 (7.5%) | 1,031 (7.6%) | 1,065 (7.8%) | 2,631 (9.3%) | 2,630 (9.3%) | 4,603 (8.5%) | 4,611 (8.5%) | 0.00 |
| Any hospitalization within prior 30 days; n (%) | 162 (1.3%) | 186 (1.5%) | 158 (1.2%) | 171 (1.3%) | 509 (1.8%) | 500 (1.8%) | 829 (1.5%) | 857 (1.6%) | -0.01 |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|----------------|----------------|---------|
| Any hospitalization during prior 31-180 days; n (%) | 802 (6.5%) | 773 (6.3%) | 898 (6.6%) | 919 (6.8%) | 2,216 (7.8%) | 2,238 (7.9%) | 3,916 (7.2%) | 3,930 (7.3%) | 0.00 |
| Endocrinologist Visit; n (%) | 2,262 (18.5%) | 2,532 (20.7%) | 2,533 (18.6%) | 2,934 (21.6%) | 6,395 (22.6%) | 7,062 (24.9%) | 11,190 (20.7%) | 12,528 (23.1%) | -0.06 |
| Endocrinologist Visit (30 days prior); n (%) | 1,446 (11.8%) | 1,557 (12.7%) | 1,734 (12.8%) | 1,932 (14.2%) | 4,097 (14.5%) | 4,318 (15.2%) | 7,277 (13.4%) | 7,807 (14.4%) | -0.03 |
| Endocrinologist Visit (31 to 180 days prior); n (%) | 1,786 (14.6%) | 1,874 (15.3%) | 1,918 (14.1%) | 2,110 (15.5%) | 5,288 (18.7%) | 5,456 (19.3%) | 8,992 (16.6%) | 9,440 (17.4%) | -0.02 |
| Internal medicine/family medicine visits; n (%) | 10,202 (83.3%) | 10,147 (82.8%) | 11,788 (86.7%) | 11,665 (85.8%) | 23,822 (84.1%) | 23,670 (83.5%) | 45,812 (84.6%) | 45,482 (83.9%) | 0.02 |
| Internal medicine/family medicine visits (30 days prior); n (%) | 7,061 (57.6%) | 7,104 (58.0%) | 8,414 (61.9%) | 8,259 (60.8%) | 15,702 (55.4%) | 15,549 (54.9%) | 31,177 (57.5%) | 30,912 (57.1%) | 0.01 |
| Internal medicine/family medicine visits (31 to 180 days prior); n (%) | 9,245 (75.5%) | 9,285 (75.8%) | 10,665 (78.5%) | 10,541 (77.6%) | 21,778 (76.9%) | 21,674 (76.5%) | 41,688 (76.9%) | 41,500 (76.6%) | 0.01 |
| Cardiologist visit; n (%) | 4,160 (34.0%) | 4,220 (34.4%) | 4,436 (32.6%) | 4,565 (33.6%) | 10,443 (36.9%) | 10,503 (37.1%) | 19,039 (35.1%) | 19,288 (35.6%) | -0.01 |
| Number of Cardiologist visits (30 days prior); n (%) | 1,419 (11.6%) | 1,400 (11.4%) | 1,393 (10.2%) | 1,516 (11.2%) | 3,361 (11.9%) | 3,349 (11.8%) | 6,173 (11.4%) | 6,265 (11.6%) | -0.01 |
| Number of Cardiologist visits (31 to 180 days prior); n (%) | 3,594 (29.3%) | 3,630 (29.6%) | 3,842 (28.3%) | 3,921 (28.8%) | 9,261 (32.7%) | 9,271 (32.7%) | 16,697 (30.8%) | 16,822 (31.0%) | 0.00 |
| Electrocardiogram; n (%) | 4,252 (34.7%) | 4,193 (34.2%) | 4,843 (35.6%) | 4,951 (36.4%) | 10,287 (36.3%) | 10,253 (36.2%) | 19,382 (35.8%) | 19,397 (35.8%) | 0.00 |
| Use of glucose test strips; n (%) | 500 (4.1%) | 503 (4.1%) | 623 (4.6%) | 615 (4.5%) | 1,140 (4.0%) | 1,101 (3.9%) | 2,263 (4.2%) | 2,219 (4.1%) | 0.01 |
| Dialysis; n (%) | 5 (0.0%) | 8 (0.1%) | 3 (0.0%) | 6 (0.0%) | 16 (0.1%) | 11 (0.0%) | 024 (0.0%) | 025 (0.0%) | #DIV/0! |
| Naive new user v8; n (%) | 2,783 (22.7%) | 2,834 (23.1%) | 2,462 (18.1%) | 2,509 (18.5%) | 4,946 (17.5%) | 4,883 (17.2%) | 10,191 (18.8%) | 10,226 (18.9%) | 0.00 |
| N antidiabetic drugs at index date | | | | | | | | | |
| ...mean (sd) | 1.74 (0.70) | 1.74 (0.72) | 1.78 (0.71) | 1.77 (0.74) | 1.77 (0.70) | 1.77 (0.71) | 1.77 (0.70) | 1.76 (0.72) | 0.01 |
| ...median [IQR] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 [1.00, 2.00] | 2.00 (0.70) | 2.00 (0.72) | 0.00 |
| number of different/distinct medication prescriptions | | | | | | | | | |
| ...mean (sd) | 11.07 (5.36) | 11.08 (5.16) | 11.05 (5.23) | 11.02 (4.89) | 11.05 (5.15) | 11.03 (4.85) | 11.05 (5.22) | 11.04 (4.93) | 0.00 |
| ...median [IQR] | 10.00 [7.00, 14.00] | 10.00 [8.00, 14.00] | 10.00 [7.00, 14.00] | 10.00 [8.00, 14.00] | 10.00 [7.00, 14.00] | 10.00 [8.00, 14.00] | 10.00 (5.22) | 10.00 (4.93) | 0.00 |
| Number of Hospitalizations | | | | | | | | | |
| ...mean (sd) | 0.09 (0.34) | 0.09 (0.34) | 0.09 (0.32) | 0.09 (0.33) | 0.12 (0.41) | 0.12 (0.41) | 0.11 (0.37) | 0.11 (0.38) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.37) | 0.00 (0.38) | 0.00 |
| Number of hospital days | | | | | | | | | |
| ...mean (sd) | 0.45 (2.24) | 0.45 (2.52) | 0.40 (1.80) | 0.43 (2.25) | 0.68 (3.01) | 0.69 (3.23) | 0.56 (2.59) | 0.57 (2.86) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (2.59) | 0.00 (2.86) | 0.00 |
| Number of Emergency Department (ED) visits | | | | | | | | | |
| ...mean (sd) | 0.40 (1.08) | 0.40 (1.20) | 0.14 (1.11) | 0.14 (1.17) | 0.47 (1.21) | 0.46 (1.22) | 0.37 (1.16) | 0.37 (1.20) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (1.16) | 0.00 (1.20) | 0.00 |
| Number of Office visits | | | | | | | | | |
| ...mean (sd) | 5.79 (4.49) | 5.80 (4.12) | 6.02 (5.06) | 6.03 (4.31) | 6.59 (5.00) | 6.58 (4.75) | 6.27 (4.90) | 6.27 (4.51) | 0.00 |
| ...median [IQR] | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 5.00 [3.00, 8.00] | 5.00 [3.00, 9.00] | 5.00 [3.00, 9.00] | 5.00 (4.90) | 5.00 (4.51) | 0.00 |
| Number of Endocrinologist visits | | | | | | | | | |
| ...mean (sd) | 0.98 (3.22) | 1.09 (3.58) | 0.91 (3.04) | 1.15 (3.71) | 1.48 (4.78) | 1.70 (5.36) | 1.22 (4.08) | 1.42 (4.62) | -0.05 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (4.08) | 0.00 (4.62) | 0.00 |
| Number of internal medicine/family medicine visits | | | | | | | | | |
| ...mean (sd) | 9.88 (14.15) | 10.31 (14.74) | 7.49 (9.52) | 7.76 (9.83) | 8.62 (12.28) | 8.76 (11.52) | 8.62 (12.12) | 8.86 (11.95) | -0.02 |
| ...median [IQR] | 6.00 [2.00, 13.00] | 6.00 [2.00, 13.00] | 5.00 [2.00, 10.00] | 5.00 [2.00, 10.00] | 5.00 [2.00, 11.00] | 5.00 [2.00, 12.00] | 5.23 (12.12) | 5.23 (11.95) | 0.00 |
| Number of Cardiologist visits | | | | | | | | | |
| ...mean (sd) | 1.76 (4.28) | 1.68 (4.00) | 1.42 (3.34) | 1.55 (3.80) | 2.04 (5.01) | 2.04 (5.04) | 1.82 (4.48) | 1.84 (4.53) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 (4.48) | 0.00 (4.53) | 0.00 |
| Number electrocardiograms received | | | | | | | | | |
| ...mean (sd) | 0.67 (1.35) | 0.67 (1.47) | 0.64 (1.21) | 0.64 (1.22) | 0.74 (1.40) | 0.72 (1.36) | 0.70 (1.34) | 0.69 (1.35) | 0.01 |
| ...median [IQR] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 (1.34) | 0.00 (1.35) | 0.00 |
| Number of HbA1c tests ordered | | | | | | | | | |
| ...mean (sd) | 1.35 (0.92) | 1.36 (0.92) | 1.13 (0.93) | 1.13 (0.93) | 1.49 (0.90) | 1.49 (0.88) | 1.37 (0.91) | 1.37 (0.90) | 0.00 |
| ...median [IQR] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 (0.91) | 1.00 (0.90) | 0.00 |
| Number of glucose tests ordered | | | | | | | | | |
| ...mean (sd) | 0.56 (2.54) | 0.57 (1.38) | 0.49 (1.40) | 0.48 (1.12) | 0.52 (1.30) | 0.53 (1.17) | 0.52 (1.68) | 0.53 (1.21) | -0.01 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 (1.68) | 0.00 (1.21) | 0.00 |
| Number of lipid tests ordered | | | | | | | | | |
| ...mean (sd) | 1.09 (1.01) | 1.08 (1.02) | 1.00 (1.40) | 1.00 (1.28) | 1.12 (0.89) | 1.11 (0.90) | 1.08 (1.07) | 1.08 (1.03) | 0.00 |
| ...median [IQR] | 1.00 [0.00, 2.00] | 1.00 [0.00, 2.00] | 1.00 [0.00, 1.00] | 1.00 [0.00, 1.00] | 1.00 [1.00, 2.00] | 1.00 [1.00, 2.00] | 1.00 (1.07) | 1.00 (1.03) | 0.00 |
| Number of creatinine tests ordered | | | | | | | | | |
| ...mean (sd) | 0.06 (0.33) | 0.06 (0.32) | 0.07 (0.39) | 0.07 (0.36) | 0.10 (0.43) | 0.10 (0.40) | 0.08 (0.40) | 0.08 (0.37) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.40) | 0.00 (0.37) | 0.00 |
| Number of BUN tests ordered | | | | | | | | | |
| ...mean (sd) | 0.04 (0.25) | 0.03 (0.24) | 0.04 (0.26) | 0.04 (0.29) | 0.06 (0.33) | 0.06 (0.30) | 0.05 (0.30) | 0.05 (0.28) | 0.00 |
| ...median [IQR] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 [0.00, 0.00] | 0.00 (0.30) | 0.00 (0.28) | 0.00 |
| Number of tests for microalbuminuria | | | | | | | | | |

Table 1: Liraglutide vs 2nd Generation Sulfonylureas

| | | | | | | | | | |
|--|--------------------|--------------------|-------------------|-------------------|--------------------|--------------------|----------------|----------------|-------|
| ...mean (sd) | 0.87 (1.24) | 0.84 (1.23) | 0.63 (1.07) | 0.62 (1.06) | 0.56 (0.81) | 0.56 (0.78) | 0.65 (0.99) | 0.64 (0.97) | 0.01 |
| ...median [IQR] | 0.00 [0.00, 2.00] | 0.00 [0.00, 2.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 [0.00, 1.00] | 0.00 (0.99) | 0.00 (0.97) | 0.00 |
| Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level | | | | | | | | | |
| ...mean (sd) | 7.11 (8.17) | 7.09 (8.36) | 2.46 (4.33) | 2.42 (4.51) | 6.66 (8.69) | 6.69 (8.92) | 5.71 (7.70) | 5.71 (7.91) | 0.00 |
| ...median [IQR] | 5.00 [0.00, 11.00] | 5.00 [0.00, 11.00] | 0.00 [0.00, 4.00] | 0.00 [0.00, 4.00] | 4.00 [0.00, 10.00] | 4.00 [0.00, 10.00] | 3.22 (7.70) | 3.22 (7.91) | 0.00 |
| Use of thiazide; n (%) | 1,601 (13.1%) | 1,597 (13.0%) | 1,648 (12.1%) | 1,695 (12.5%) | 4,220 (14.9%) | 4,168 (14.7%) | 7,469 (13.8%) | 7,460 (13.8%) | 0.00 |
| Use of beta blockers; n (%) | 5,279 (43.1%) | 5,288 (43.2%) | 5,784 (42.6%) | 5,886 (43.3%) | 13,340 (47.1%) | 13,381 (47.2%) | 24,403 (45.0%) | 24,555 (45.3%) | -0.01 |
| Use of calcium channel blockers; n (%) | 3,483 (28.4%) | 3,522 (28.7%) | 3,883 (28.6%) | 3,851 (28.3%) | 8,623 (30.4%) | 8,726 (30.8%) | 15,989 (29.5%) | 16,099 (29.7%) | 0.00 |